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ORIGINAL CONTRIBUTIONS

Volume 22 December, 1955 Number 12

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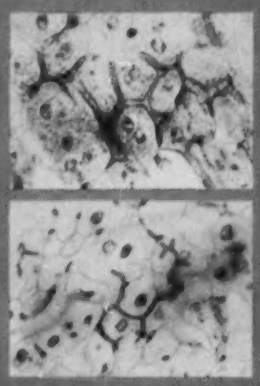

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(1) Clara, M.: Med. Monatsschr. *7*:356, 1953. (2) Brauer, R. W., and Pessotti, R. L.: Science *115*:142, 1952. (3) Schwimmer, D.; Boyd, L. J., and Rubin, S. H.: Bull. New York M. Coll. *16*:102, 1953.

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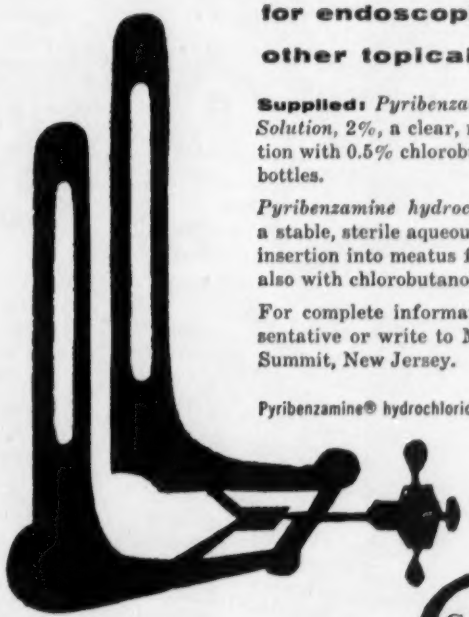

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THE ILEO-CECAL VALVE IN DISEASES

S. L. Beranbaum, M. D., and Kakarla Subbarao, M. D.,* New York, N. Y.

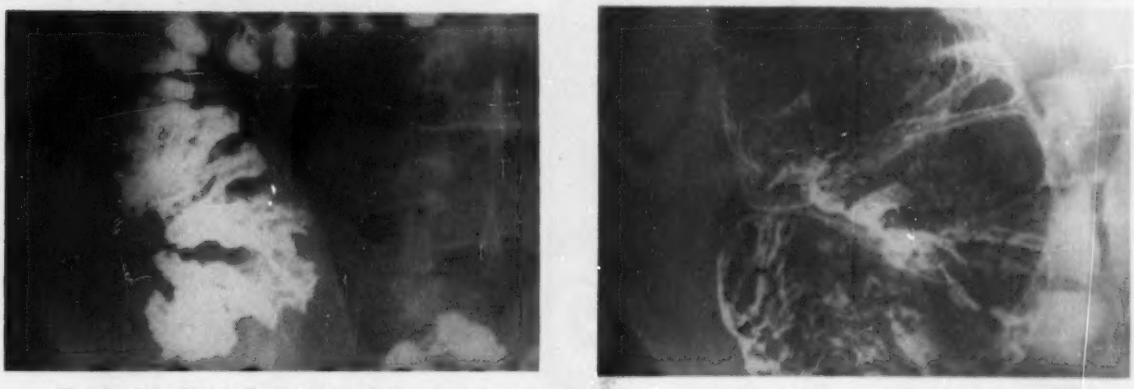

Fig. 1a & b. Unusually located and distorted ileocecal valve due to post-appendectomy adhesions. In (a) the post-evacuation exposure, the cecum is rotated. The air contrast exposure (b) illustrates the ileocecal valve on the lateral aspect of the bowel with the caput of the cecum also directed laterally and superiorly.

WITH an appreciation of the roentgenological appearance of the normal ileo-cecal valve and its hypertrophied variations, a brief study of the valve in various diseases was undertaken. Disease of the ileo-cecal valve proper is rather rare. We have not encountered any such case, although in one instance of submucous lipoma the origin of the lipoma is debatable. (Fig. XI).

Isolated articles have been appearing in the literature from time to time describing lesions of the valve proper. Wiener and Polayes have described a case of ileo-cecal submucous lipoma discovered at necropsy. Glasser and Mersheimmer have described a case of carcinoma of ileo-cecal valve and while reviewing the literature, they stressed the importance of statistical error in reporting any carcinoma of the ileo-cecal region as carcinoma of ileo-cecal valve. Ross Golden in his article on enlargement of the ileo-cecal valve describes as one of the causes to be submucous fatty infiltration of the valve. Rigler has added to the growing list of demonstrable abnormalities of the ileo-cecal valve, an unusual case of prolapse of the lower lip into the terminal ileum simulating a prolapsing polyp.

The ileo-cecal valve might be disturbed, disfigured and disorganized both anatomically and functionally due to a variety of diseases affecting that region. When the surrounding pathological process is recognized, it is not difficult to study and identify the mutilated ileo-cecal valve. The following is a brief description of the appearances of the valve in the different pathological processes as observed roentgenologically.

Post Operative Adhesions

Adhesions may distort the normal anatomy and thus present an unusual roentgenological appearance of the

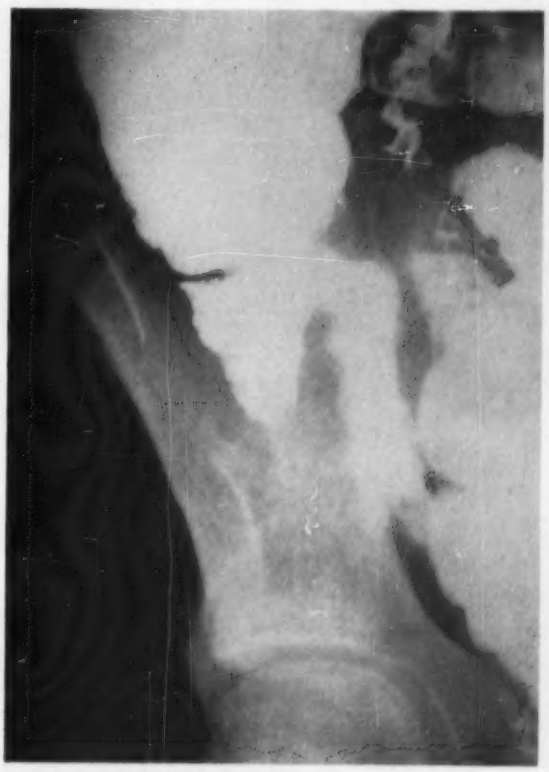

Fig. 2. Early terminal ileitis with irregular erosions of the ileal mucosa. The ileocecal valve shows minimal, if any, involvement.

*James Picker Foundation Fellow in Radiological Research. University Hospital, New York University, Bellevue Medical Center.

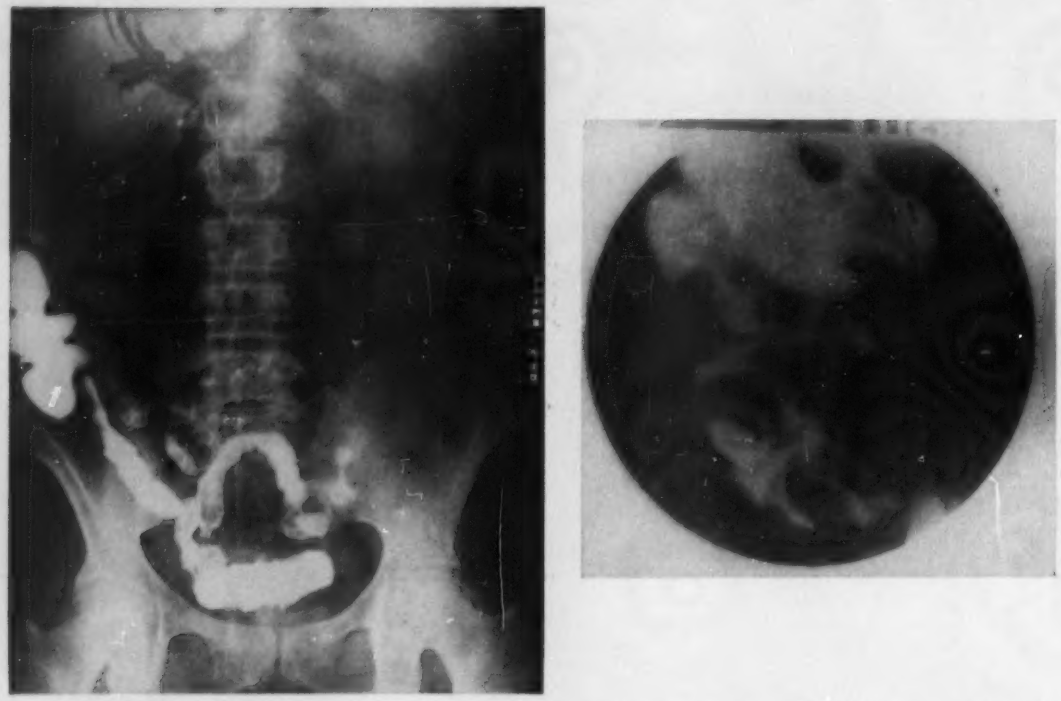

Fig. 3a & b. Terminal ileitis with hypertrophy of the ileocecal valve, best illustrated in the pressure film (b).

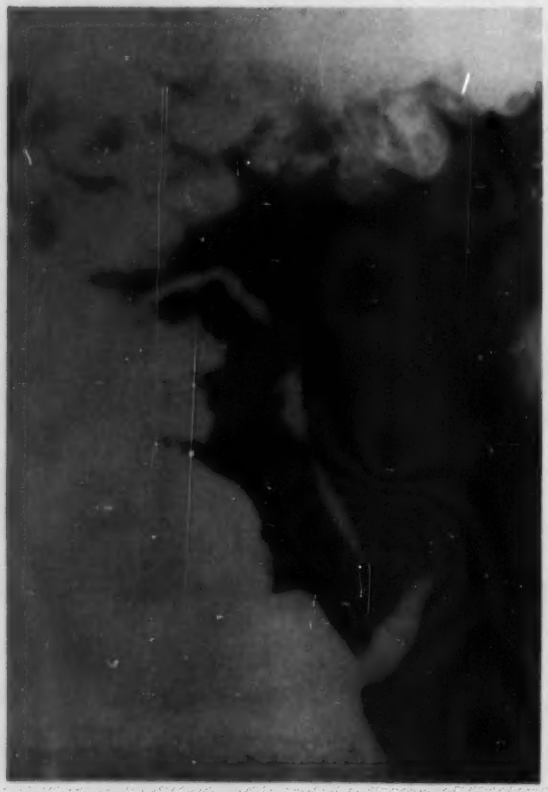

Fig. 4. Advanced terminal ileitis in the stenotic stage with an atrophied ileocecal valve.

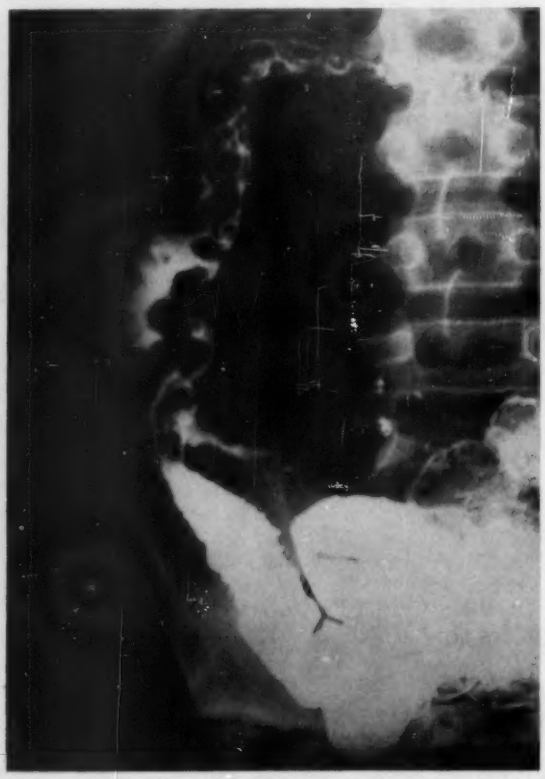

Fig. 5. Ileo-colitis with large lips of the ileocecal valve.

valve and sometimes may even displace it, so that it is seen in unusual locations (Fig. I). Awareness of this condition and history of previous surgery will have an otherwise perplexing problem.

TERMINAL ILEITIS

In cases of terminal ileitis, the ileo-cecal valve in early stages is not involved, but as the disease progresses, a series of changes may take place in the ileo-cecal valve. In the acute stage, there may be edema and inflammatory changes in the lips which radiologically may present a large defect. This condition is readily differentiated from hypertrophy by recognition of the presence of disease in the adjacent loops of ileum. As the primary disease becomes chronic with cicatricial changes, the valve may also be involved in the same process with atrophy and fibrosis resulting in a thin atrophic valve. This is manifested roentgenologically as a continuous channel from the ileum to the cecum, without any demarcation by the lips. As seen functionally, the tone is decreased and ileo-cecal incompetency ensues readily during a barium enema examination (Fig. IX).

ENTEROCOLITIS AND ULCERATIVE COLITIS

In cases of enterocolitis and ulcerative colitis, a similar chronological cycle is present, namely, a normal valve, an enlarged valve and an atrophied valve, the appearance being predicated on the particular stage of the disease. The pseudopolypi observed as a result of piling up the mucosa in later stages of ulcerative colitis may be present on the lips of the valve, producing an exaggerated filling defect (Fig. V).

ILEOCECAL TUBERCULOSIS

The appearance of the ileocecal valve in tuberculosis has been presented by Gershon-Cohen and Kremens in a very lucid manner. They emphasized that whereas

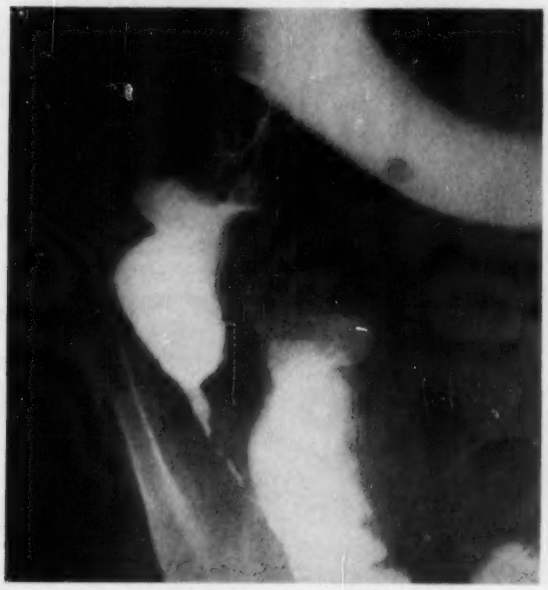

Fig. 6. Ileo-colitis with atrophied lips of the ileocecal valve.

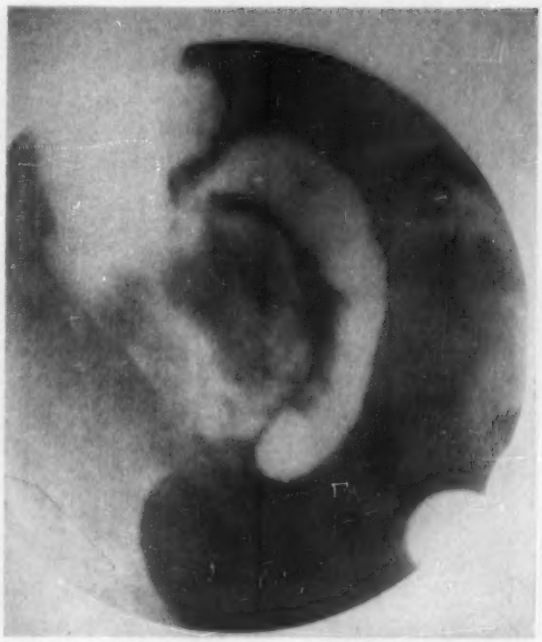

Fig 7. A case of ulcerative colitis with normal ileocecal valve. The defects in the cecum are caused by intestinal content.

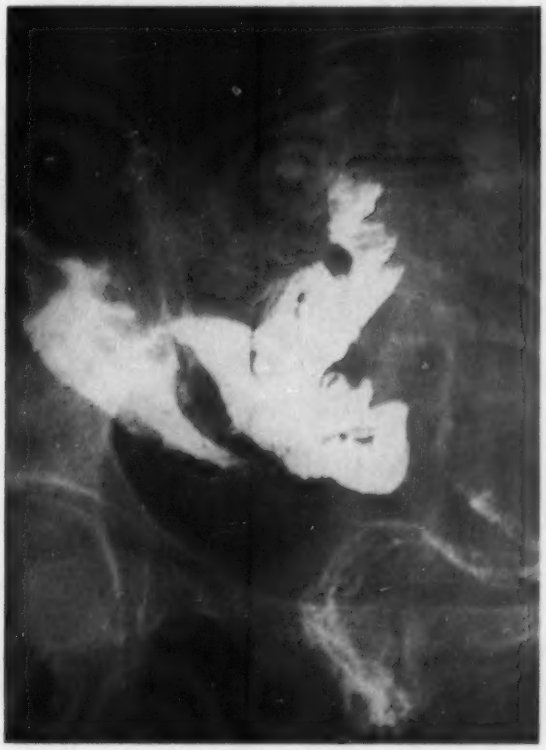

Fig. 8. A case of ulcerative colitis with large lips of the ileocecal valve.

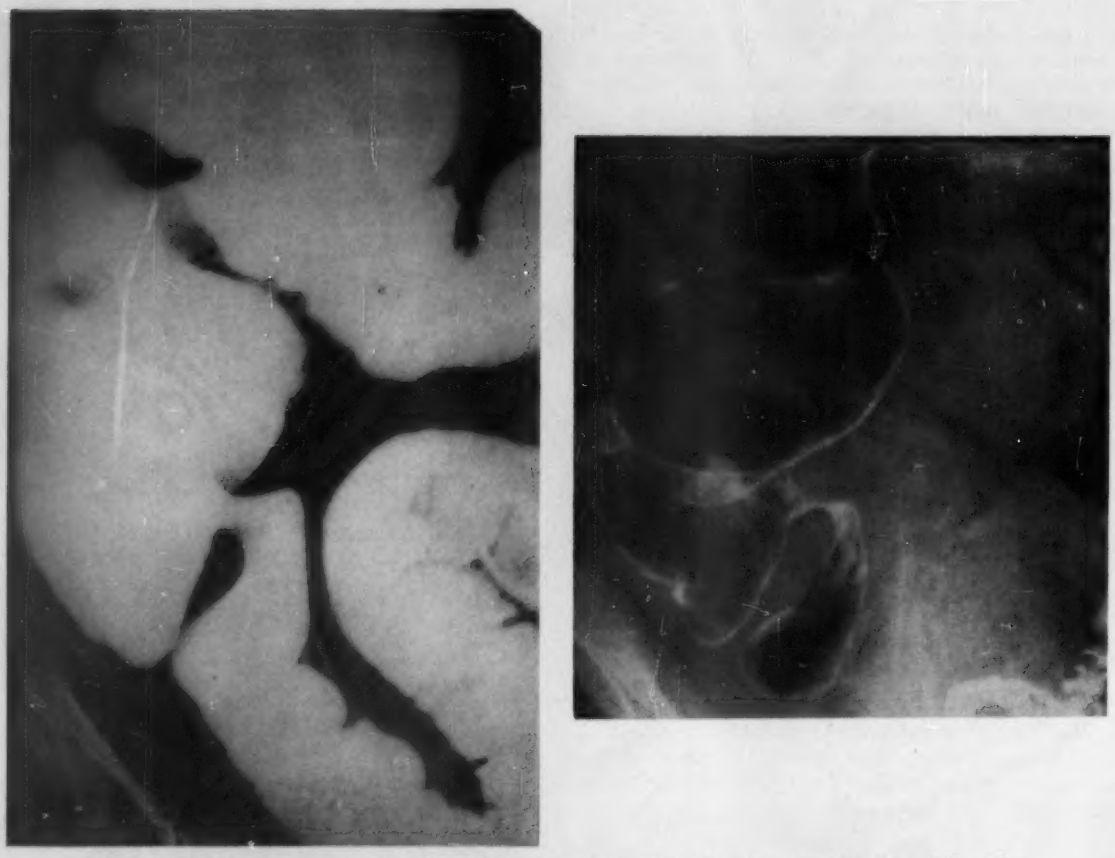

Fig. 9a and b. A case of chronic ulcerative colitis of long standing with atrophied lips of the valve.

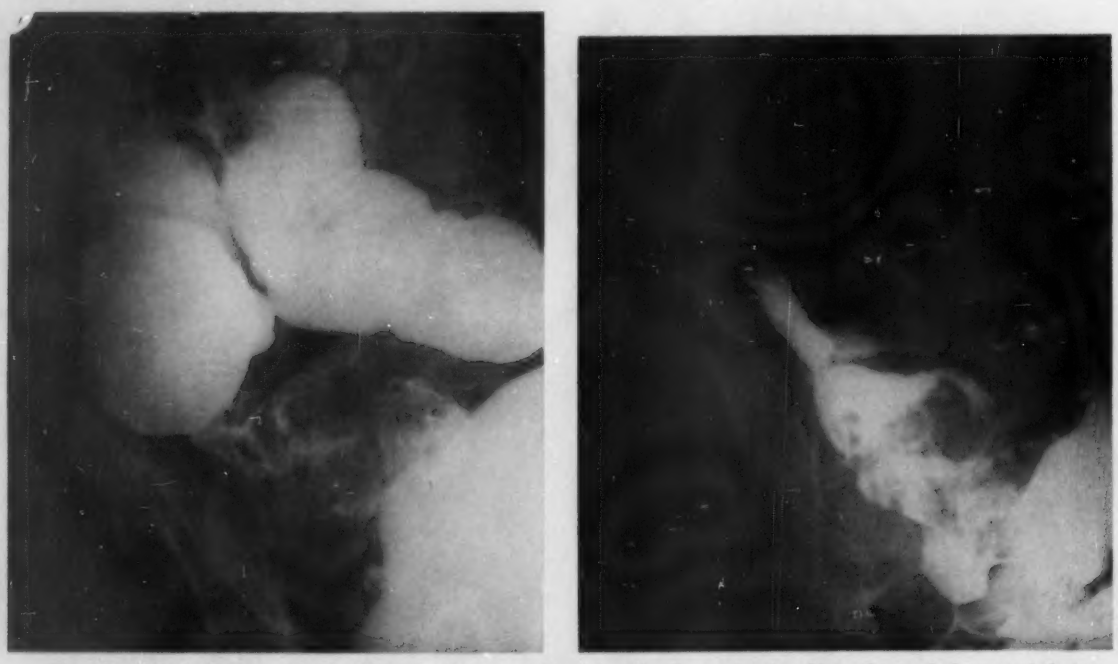

Fig. 10a & b. A large neoplastic defect in the cecum involving the ileocecal valve. Note the marked mucosal destruction. Compare with the previously presented appearance of the hypertrophied valve.

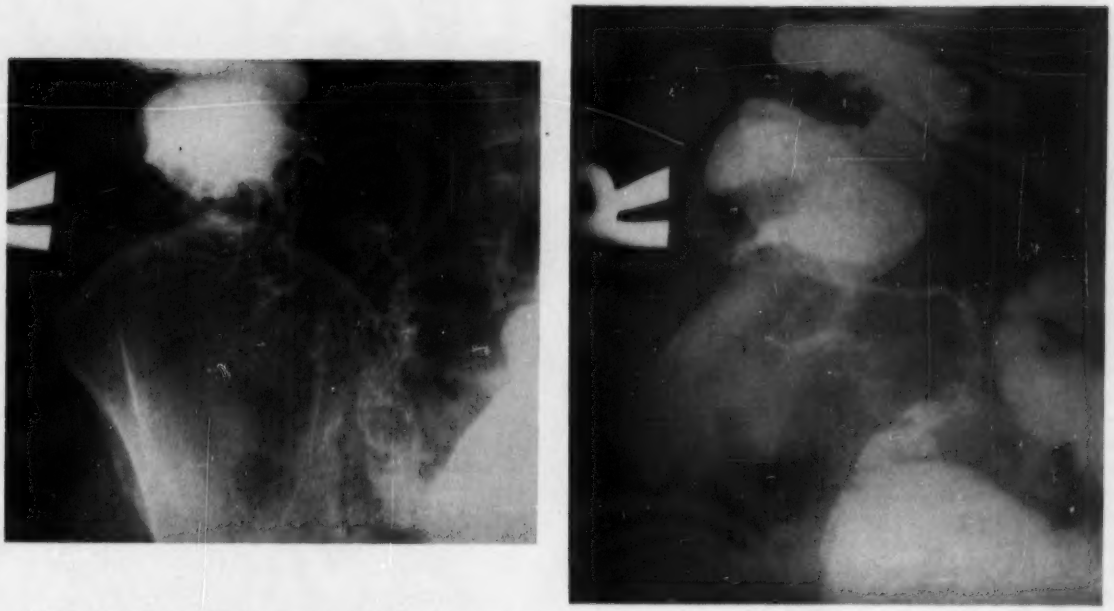

Fig. 11a & b. S.A., a 54-year-old white male complaining of crampy lower abdominal pain of 3 weeks duration with melena. The radiographic features illustrate an enlargement at the ileocecal valve with a larger nodular appearance. The official radiographic interpretation ended with the following discussion.

"There is undoubtedly a defect at the ileocecal region which probably represents a hypertrophied ileocecal valve, but an actual neoplasm cannot be ruled out. The patient deserved an exploratory final diagnosis."

The operative report reads in part—"On cecotomy the ileocecal valve was redundant, non-ulcerative with a superior pole (meaning lip) submucous lipoma approximately 5 cm. in diameter. The polyp was smooth on a short stalk above the valve on the posterior cecal wall, approximately 0.8 cm. in diameter." Whether or not the lipoma should be categorized as a primary lesion of the ileocecal valve is debatable. This case demonstrates the difficulties the radiologist may encounter and cautions against a too dogmatic opinion.

the apex of the usual ileocecal valve defect points inwardly toward the lumen of the cecum, in cases of tuberculosis, the apex is directed towards the ileum. This defect, also called "inverted umbrella" by Fleischner, although thought to be quite characteristic of tuberculosis, it has been observed, in our limited experience in other chronic inflammatory processes involving the valve (Fig. IX). This sign is probably not specific to tuberculosis.

NEOPLASMS

Neoplasms involving and infiltrating the ileocecal valve are not uncommon. The peremptory evidence of the source of the primary neoplasm is most difficult to ascertain because of the fact that these lesions are nearly always seen at a late stage in the course of the disease. By that time, the ileocecal valve is invariably involved. The important feature is to differentiate a benign from a malignant lesion. The pertinent differential points have already been presented, namely, the irregularity of the lesion and the constancy of the findings in a series of examinations.

PROLAPSE AND INTUSSUSCEPTION

The study of the ileocecal valve is not complete, unless we consider the conditions of prolapse of the ileocecal valve into the cecum as well as the intussusception of the terminal ileum. These two conditions are of one and the same pathological process, though there is difference in degree. The appearances of the prolapse of the ileocecal valve have been discussed in the previous article. Usually, in all cases of intussusceptions, there appears to be a primary source either in the ileocecal valve proper or in the terminal ileum, viz.: a polyp, a lipoma or some other similar cause. The roentgenological manifestations and their criteria in arriving at a definite diagnosis of intussusception are well known and do not come under the scale of this present article.

SUMMARY

A brief discussion of the roentgen appearances of ileocecal valve, in various pathological processes of the ileocecal region has been made with description of the conditions that affect the valve.

The authors wish to express their appreciation to Dr. Maxwell H. Poppel, Professor of Radiology, for his stimulating help and constructive criticism.

REFERENCES

1. Fleischner, F. G. and Bernstein, C.: Roentgen-Anatomical Studies of the Normal Ileocecal Valve. Radiology Vol. 54, No. 1, pages 43-58. January, 1950.
2. Glasser, S. T. and Merscheimmer, W.: Carcinoma of the Ileocecal Valve. Am. J. Surgery, Vol. 56, No. 3, 1942, pages 650-654.
3. Gershon-Cohen J. and Kremens, J.: X-ray Studies of the Ileocecal Valve in Ileocecal Tuberculosis. Radiology, Feb., 1954, pages 251-254.
4. Golden, R.: Enlargement of Ileocecal Valve. Am. J. Roentgen & Radium Therapy, Vol. 50, 1943, pages 19-23.
5. Rigler, Leo G. and Lasser, E.: Prolapse of the Lower Lip of the Ileocecal Valve into the Terminal Ileum. Am. J. Roent. and Radium Therapy, Vol. 65, 1951, pages 878-881.

ON THE COMPARISON BETWEEN GASTRIC SUCTION BIOPSIES AND GASTROSCOPY

RUDOLF SCHINDLER, M. D., F. A. C. P. Los Angeles, Calif.

THE ADVENT of suction biopsy has made possible the histologic study of small pieces of the gastric mucosa (7,9,10). The results of such biopsies have sometimes been compared with the gastroscopic picture (2-6). If there is disagreement, the gastroscopic impression is thought to be in error. Comparison of such biopsies with autopsy findings have led, however, to serious objections (Desneux, 1). In about 120 suction biopsies done with the Australian suction biopsy instrument I have often found the above mentioned disturbing discrepancy. However, it must be remembered that different results were obtained from the study of large biopsies taken at laparotomy (8). There was almost always a complete agreement between gastroscopic and microscopic picture. One must suspect that the tiny pieces obtained blindly by suction biopsy are simply too small to represent the true picture of the gastric mucosa, even if multiple samples are taken, with the exception perhaps of such cases in which the mucosa is uniformly damaged, as after x-ray irradiation (2,4).

The following case tends to confirm this view.

A 43 year old woman had "gas attacks" in the abdomen, following a hysterectomy. She had nausea and vomiting, but no severe pain. The gallbladder was removed, but no stones were found. Again attacks of abdominal distress occurred during which she "could not see a thing." All laboratory tests were reported to be negative, except that gastric analysis revealed no acid. She was then referred for gastroscopy. From the case history I believed I was dealing with a severe psychoneurosis, but gastroscopy had a surprising result: "The mucosa of the antrum showed extremely severe changes with extensive soft swelling and node formation, especially in the posterior wall. Everywhere there were small longitudinal hemorrhages within the swollen mucosa. No real stiffness was seen. Some swelling was seen above the angulus and there was one hemispherical hemorrhagic protrusion. Swelling was seen along the posterior wall and lots of small hemorrhages were seen along the posterior wall and within the swollen folds. Two tiny erosions were observed at the top of the folds. The anterior wall and lesser curvature showed extensive thinning with the appearance of blood vessels. — Impression: Extremely severe and unusual form of chronic atrophic hemorrhagic erosive gastritis. (Lymphoblastoma cannot be excluded with the last degree of certainty; however, the stiffness of the folds usually seen in the lymphoblastoma was not present)."

Two biopsies were taken with the Australian suction instrument from a rather distal region of the stomach. — In addition, however, a large piece of tissue was recovered from the Ewald tube through which the stomach had been drained preceding gastroscopy.

The section obtained by suction biopsy shows the whole depth of the gastric mucosa (Fig.1). There is no atrophy, the glands are undisturbed. The only impressive changes are below the surface epithelium and between the pits. There is edema, in which one finds fibroblasts and plasma cells. This is the picture of chronic superficial gastritis. The severe changes seen gastroscopically did not appear in these biopsies.

Entirely different was the histologic picture of the piece of tissue recovered from the Ewald tube (Fig. 2-3). Extensive destruction of glands is seen. There is interstitial infiltration, consisting of small round cells and plasma cells. In some places clusters of polymorphonuclear cells predominate. Within the infiltration iso-

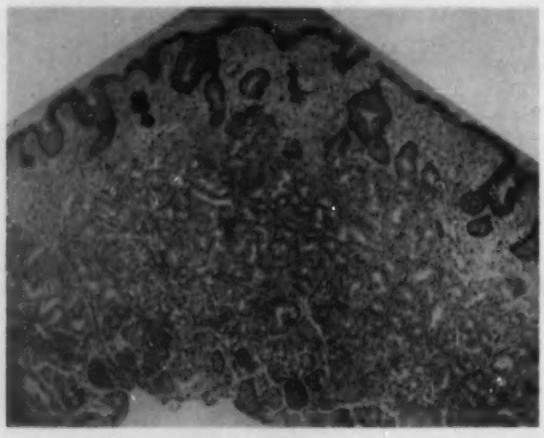

Fig. 1 Microscopic section obtained by suction biopsy, revealing only superficial gastritis. No agreement with the gastroscopic findings.

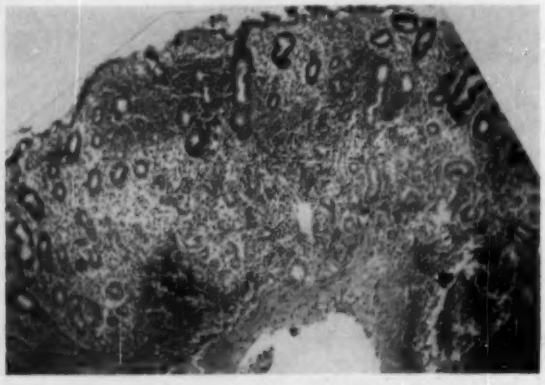

Fig. 2 Microscopic section from spontaneously eliminated piece of gastric mucosa. Full agreement with gastroscopic findings. Extensive severe atrophic hemorrhagic erosive gastritis.

lated parietal cells are found. There is superficial ulceration of the surface epithelium. Many polymorphonuclear leucocytes are seen to migrate through the surface epithelium. Bacterial colonies lie on purulent exudate in the base of the ulcers.

Thus, the microscopic picture of this spontaneously eliminated piece of tissue confirms fully the gross picture seen at gastroscopy and proves that the patient has an unusually severe chronic ulcerative inflammation of the stomach.

The suction biopsy does not show such a picture. It only reveals a chronic superficial gastritis which clinically might cause symptoms, but could not be considered as a serious disease.

SUMMARY

1. A case of unusually severe atrophic ulcerative gastritis is presented in which suction biopsy sections were not in agreement with the gross gastroscopic findings. A spontaneously eliminated piece of gastric mucosa, however, revealed a microscopic picture in conformity with the gross gastroscopic picture.

2. Suction biopsy sections, though often clinically valuable, should be used for research purposes with great reservation only, even if multiple biopsies are taken. The pieces are too small to permit cogent conclusions as to the structure of the gastric muçosa as a whole. Since the specimens are taken blindly it is impossible to be sure that the biopsy is taken from the diseased area.

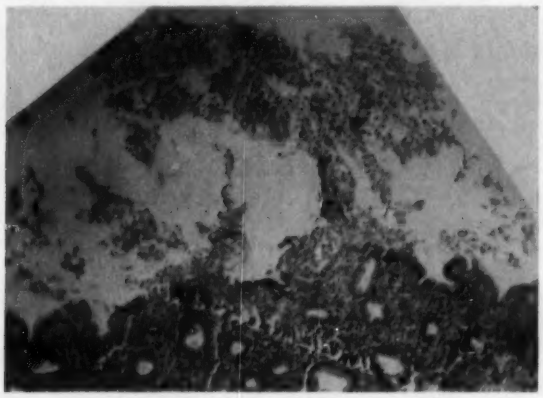

Fig. 3 Another area from the section pictured in Fig. 2. "Smoke-stack" erosion.

REFERENCES

1. Desneux, J. J., Réflexions sur les biopsies gastriques par la méthode australienne. Acta gastro-enterologica Belgica, 17:7, 1954.

2. Doig, R. K.; Funder, I. F.; and Weiden, S., Serial gastric biopsy studies in a case of duodenal ulcer treated by deep-ray therapy. M. J. Australia, 38:828, 1951.

3. ....., and Motteran, R., The histology of gastritis. Austral. and New Zealand J. of Surg., 19:296, 1950.

4. Goldgraber, M. B.; Rubin, C. E., Palmer, W. L.; Dobson, R. L.; and Massey, B. W., The early gastric response to irradiation, a serial biopsy study. Gastroenterology, 27:1, 1954.

5. Palmer, E. D., Error in gastroscopic diagnosis. Gastroenterology, 16:341, 1950.

6. ....., Gastric mucosal biopsy findings correlated with gastroscopic diagnoses. Am. Med. Soc., 219:648, 1950.

7. Rubin, C. E.; Goldgraber, M. B.; and Smith, C., An improved gastric biopsy tube. Gastroenterology, 25:31, 1953.

8. Schindler, R., Gastritis. New York: Grune and Stratton, 1947.

9. Tomenius, J., An instrument for gastrobiopsies. Gastroenterology, 15:498, 1950.

10. Wood, I. J.; Doig, R. K.; Motteram, R.; and Hughs, A., Gastric biopsy. Lancet, 1:18, 1949.

THE ACTION OF RESERPINE ON THE MOTILITY OF THE DIGESTIVE TRACT

A. J. PLUMMER, W. E. BARRETT AND R. RUTLEDGE Summit, N. J.

IN 1952 Muller, Schlittler and Bein (5) reported the isolation of a crystalline alkaloid from the roots of Rauwolfia serpentina Benth. This alkaloid, which was named reserpine, was first studied for its characteristic pharmacological properties by Muller, Schlittler and Bein (5), by Bein (3,4), and later by Plummer et al (6,7), by Schneider et al (9) and by Trapold, Plummer and Yonkman (10). Reserpine has been found to possess the hypotensive and sedative activity found in the Rauwolfia serpentina roots. Its most fundamental action appears to be a decrease in central sympathetic activity (3). Its mechanism and site of action within the central nervous system have been studied in some detail by Schneider et al (9) and by Bein (4).

This report deals with the effect of reserpine on the gastrointestinal tract of various species of animals. This subject is of interest, as diarrhea is commonly observed following the administration of reserpine, especially in the dog, cat and rabbit, though, fortunately, rarely in the human. A recent preliminary report of this work has appeared (Barrett, 2).

Research Department, Ciba Pharmaceutical Products, Inc. Summit, New Jersey.

Submitted June 15, 1955.

METHODS

A. *Studies on Isolated Tissues.*

Segments of the isolated ileum of the guinea pig, rabbit, cat and dog were suspended in a modified Locke's solution contained in the glass isolated tissue

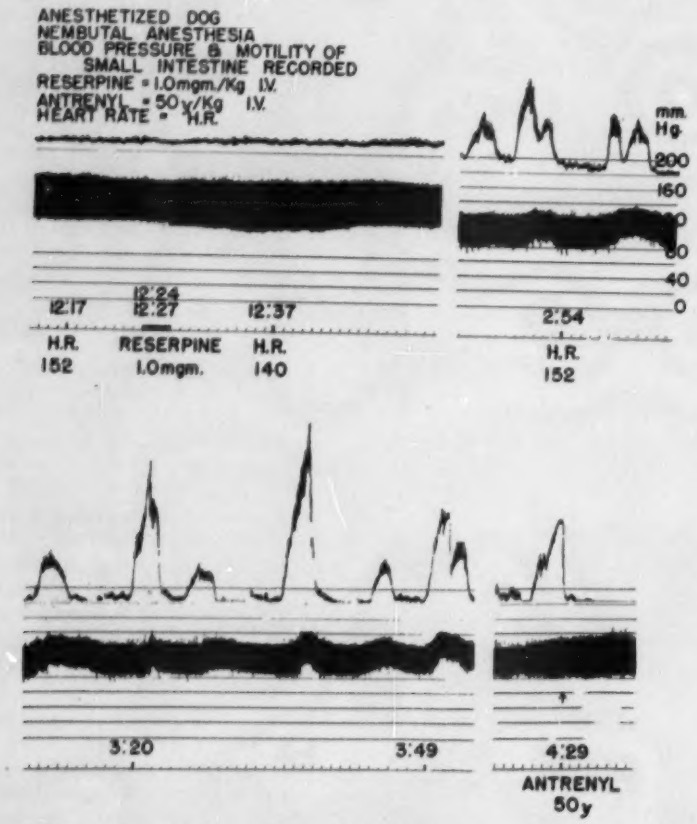

Fig. 1 The stimulatory action of reserpine on the small intestine of the nembutalized dog.

baths described by Anderson, Barrett and Craver (1), and the influence of reserpine on these tissues was recorded kymographically. Similarly, the effects of reserpine on the isolated colon of the rabbit, rat, cat and dog were studied.

B. *Anesthetized Dog Preparations*

1. *Anesthetized Dogs with Intact Vagi.* Dogs were anesthetized with Nembutal and the activity of the small intestine was studied by means of a balloon placed in the small intestine through a midline abdominal incision. Intestinal movements were recorded kymographically by connecting the balloon to a water-filled manometer. The femoral arterial blood pressure was recorded. The femoral vein was cannulated and all drugs were administered by this route.

2. *Anesthetized Dogs with Cervical Vagotomy.* The procedure for this experimental preparation was the same as that described for the anesthetized dog with the intact vagus, except that both vagus nerves were ligated and divided at the cervical region.

3. *Anesthetized Dogs with Transabdominal Vagotomy.* This experimental procedure was the same as that listed above, except that both vagus nerves were crushed and severed, and the esophagus was ligated at the cardiac region of the stomach. The motility of the small intestine was recorded by means of a balloon attached to a water manometer. In those experiments in which vagal stimulation was employed, the stimulation was accomplished with an Electrodyne stimulator by means of electrodes attached to the vagus nerves in the cervical region.

4. *Anesthetized Vagotomized Spinal Dogs.* Dogs were anesthetized with Nembutal and the cervical spinal cord isolated and cut by means of cautery at C-6. In addition to transection of the spinal cord at C-6, both vagus nerves were severed in the cervical region. The animals were immediately placed on artificial respiration after the transection of the spinal cord. The motility of the small intestine in these spinal animals was recorded by means of a balloon inserted into the small intestine and attached to a water manometer. The blood pressure was recorded from the femoral artery and all drug injections were made into the cannulated femoral vein.

Since reserpine is practically insoluble in aqueous solution, the reserpine employed in all these experiments was dissolved in a vehicle which consisted of 25 per cent ethyl alcohol, 25 per cent propylene glycol and 50 per cent water. The maximum concentration of the reserpine obtained in this vehicle was a 0.1 per cent solution. The effect of the vehicle itself was studied in all the experiments described in this report, in order to

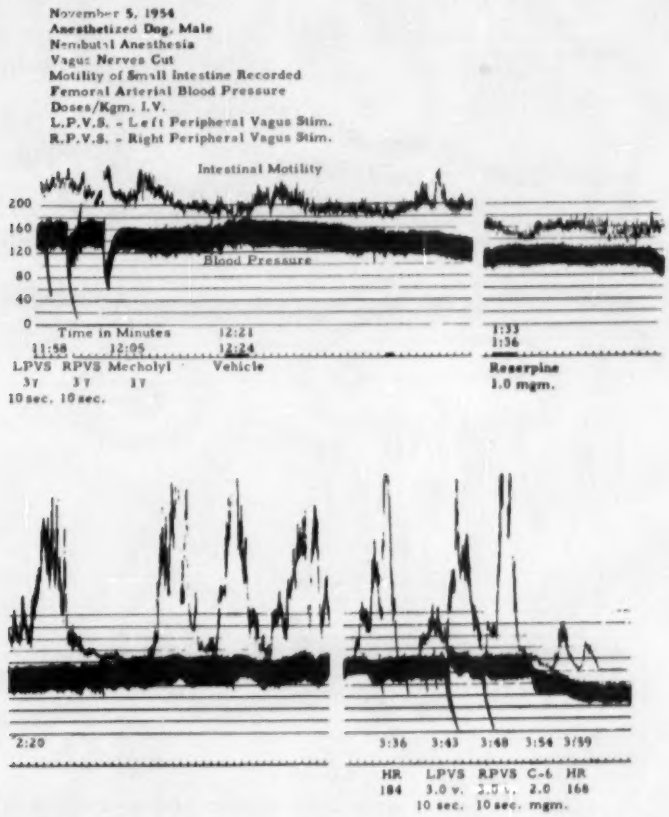

Fig. 2 The stimulatory action of reserpine on the small intestine of the nembutalized dog subjected to bilateral cervical vagotomy.

make certain that the vehicle was not responsible for the activity noted. Hexamethonium chloride and Antrenyl (R) bromide were employed in an effort to antagonize the effects of reserpine.

RESULTS

The effect of reserpine was studied on the isolated ileum and colon of various species of animals after adding measured volumes of a solution of the drug to the bath in which the tissue was suspended. The results obtained with the isolated tissues are summarized in Table 1.

When tested on the isolated ileum of the guinea pig, reserpine exhibited anticholinergic and antihistaminic activity, but this activity did not become apparent until

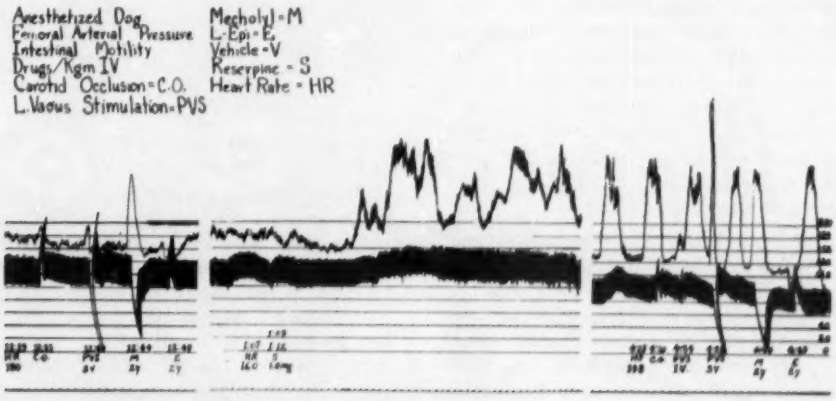

Fig. 3 Increased motility and increased sensitivity to faradization of the small intestine of the nembutalized dog following the administration of reserpine.

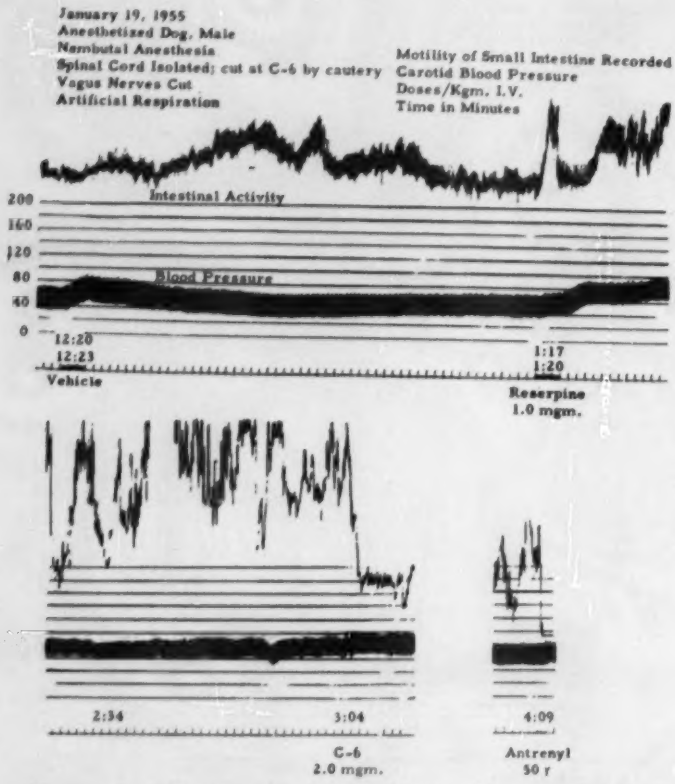

Fig. 4 Increased motility of the small intestine following reserpine in the nembutalized dog subjected to a transection of the spinal cord at C-6 and to cervical vagotomy.

a concentration of 10 microgm./ml. of reserpine was reached. With the isolated ileum of the rabbit as a test object, reserpine in doses of 1 and 10 microgm./ml. exhibited marked anticholinergic activity (Table 1). In addition, these doses of reserpine *per se* caused a slow, progressive relaxation or inhibition of the spontaneous activity of the rabbit ileum. When tested on the isolated ileum of the cat and the dog, reserpine in doses of 1 and 10 microgm./ml. caused either no relaxation or slight diminution of the spontaneous activity. No anticholinergic properties were observed at the same dose level when tested on the isolated ileum of the cat. Reserpine in a dose of 10 microgm./ml., when tested on the isolated ileum of the dog, exhibited anticholinergic activity. No stimulatory or cholinergic-type activity was noted in any species. Concentrations of reserpine below 1 microgm./ml. were without effect of any kind on the isolated ileum of any species studied.

When the isolated colon of the rabbit, rat, cat or dog was employed as the test object, reserpine did not exhibit cholinergic-type activity. Reserpine at a dose of 10 microgm./ml. usually caused a relaxation of the isolated colon obtained from the various species. Anticholinergic activity appeared when reserpine was tested against the isolated colon of the rat at a dose of 10 microgm./ml. When tested against acetylcholine-induced contraction of the isolated colon of the other species, reserpine did not appear to possess any appreciable antagonistic activity.

In contrast to the isolated tissue studies, reserpine in the Nembutal-anesthetized dog had the following effects:

(1) In the anesthetized dog with intact vagus nerves, reserpine elicited stimulation of the small intestine after an intravenous dose of 1 mgm./kgm. (Figure 1).

(2) In observations with the anesthetized dog subjected to cervical vagotomy, reserpine in a dose of 1 mgm./kgm. intravenously produced a stimulation of the small intestine (Figure 2). When studied in the anesthetized dog which had been subjected to a transabdominal vagotomy, reserpine also evoked a stimulation of the small intestine.

In addition to a stimulation in the preparations just mentioned, reserpine appeared to increase the sensitivity of the small intestine to vagal stimulation, and usually, but not consistently (Figure 3) without a concomitant increase in the sensitivity of the intestine to mecholyl. Furthermore, this stimulation of the intestine by reserpine usually occurred before a drop in the blood pressure appeared. The stimulation caused by reserpine in the intact and vagotomized anesthetized dog usually occurred after a latent period of from one-half to three hours following the administration of the reserpine. The

TABLE 1

EFFECT OF RESERPINE ON THE SMOOTH MUSCLE OF ISOLATED ORGANS

	RESERPINE		vs. ACETYLCHOLINE	
Isolated Organ	Dose Microgm./ml.	Effect	Dose Microgm./ml.	Per Cent Inhibition
Guinea pig ileum	1	Slight relaxation	0.2	0
	10	Relaxation	0.2	70-90
Rabbit ileum	1	Relaxation	0.02	88
	10	Relaxation	0.02	98-100
Rat ileum	1	Slight relaxation	0.2	48
	10	Relaxation	0.2	85-100
Cat ileum	1	0-Slight relaxation	0.2	0
	10	Slight relaxation	0.2	12
Dog ileum	1	0	0.2	20
	10	Relaxation	0.2	95-100
Rabbit colon	1	0	0.02	0
	10	Relaxation	0.02	0-25
Rat colon	1	Slight relaxation	0.2	20-35
	10	Slight relaxation	0.2	50-80
Cat colon	1	0	1.0	0
	10	None or slight stimulation—relaxation	1.0	0-25 avg. 8
Dog colon	1	0	1.0	0
	10	Relaxation	1.0	10

	vs. HISTAMINE	
	Dose Microgm./ml.	Per Cent Inhibition
Guinea Pig ileum	0.6	0-20
	0.6	50-90

vehicle was administered to the anesthetized dog as a control in each experiment prior to the injection of the reserpine and did not cause a stimulation of the small intestine. Both reserpine and the vehicle were injected slowly over a three-minute interval. In Figure 2 it will be noted that hexamethonium in a dose of 2 mgm./kgm., administered intravenously, greatly decreased the stimulation following reserpine administration. Figure 4 illustrates that after vagotomy a stimulation of the small intestine caused by reserpine was inhibited by Antrenyl, a potent anticholinergic agent (8).

In the anesthetized dog subjected to a transection of the spinal cord at C-6 and a cervical vagotomy (Figure 4), reserpine administered in a dose of 1 mgm./kgm. intravenously, caused a stimulation of the small intestine. The time of onset for stimulation averaged, for five experiments, 1.2 hours (with a range of from eleven minutes to two hours and fifteen minutes). Figure 4 typifies some of the results obtained in the spinal animals and, once again, it will be noted that hexamethonium in a dose of 2 mgm./kgm., administered intravenously, caused a marked inhibition of the stimulation elicited by reserpine.

DISCUSSION

Reserpine has been found to cause a marked increase of the motor activity of the small intestine. Studies with the isolated ileum and the isolated colon of various species, including the dog, provided no evidence that reserpine possessed a direct stimulatory type of activity, at least in doses of 1 and 10 microgm./ml. of bath volume. It was considered that possibly these doses of reserpine employed in isolated tissue studies were in excess of those occurring *in vivo* and thus even the dose of 1 microgm. of reserpine per milliliter of bath volume might mask a stimulatory effect associated with a lower concentration. This has been shown not to be true, however, for with the rabbit gut as a test object concentrations between 0.001 and 0.1 microgm./ml. in the tissue bath were without effect of any kind, even after prolonged contact.

Another possible explanation for the difference between the results obtained with the isolated tissues and those in the anesthetized and unanesthetized dogs is that reserpine may be altered in the body of the intact animal before its usual hypotensive and sedative activity appears and before any signs of increased intestinal activity appear. This would seem plausible when it is realized that in the anesthetized dog stimulation of the small intestine by reserpine does not occur immediately after the drug is administered intravenously but usually after a latent period of an hour or more. In the unanesthetized dog, too, diarrhea which follows reserpine comes on some hours after the administration of the drug. The delay may simply be a reflection of

the time required for tissue deposition rather than metabolism.

The results obtained with the anesthetized dog indicate that reserpine causes a stimulation of the small intestine after both cervical vagotomy and transabdominal vagotomy which usually occurs before a marked fall in blood pressure ensues. This indicates that in the range of doses employed in these studies a stimulation of the small intestine by reserpine does not require a complete parasympathetic nervous pathway between the central nervous system and the periphery.

In order to assess the role that decreased sympathetic tone induced by reserpine might play in increasing the activity of the gastrointestinal tract, anesthetized dogs were subjected to transection of the cord at C-6, as well as to cervical vagotomy. With this preparation, in which the effect of sympathetic tone has been removed, reserpine in an intravenous dose of 1 mgm./kgm. also caused a stimulation of the small intestine which was markedly decreased by 2 mgm./kgm. of the ganglionic blocking agent, hexamethonium, given intravenously. These experimental results appear to indicate that it is not the decreased central sympathetic predominance alone occurring after reserpine which is responsible for the stimulation of the gastrointestinal tract, but rather that reserpine has, in addition, a more peripheral stimulatory action. The inhibition of reserpine-induced stimulation by hexamethonium, a ganglionic blocking agent, or by Antrenyl, an anticholinergic agent, suggests that this peripheral site of stimulation may be located within the parasympathetic ganglia, although there exists the possibility of an action on the sympathetic system at a level below the cord transection. The only reported action of reserpine on the cord has been one of facilitation of somatic reflex activity by Schneider (9). A stimulation of this region, therefore, would be expected to cause inhibition rather than the observed stimulation of the intestine.

SUMMARY

1. Studies have been designed to determine the cause of the increased motor activity of the intestine caused by reserpine in animals. When reserpine was tested on the isolated ileum of various species of animals, it was found to possess moderate anticholinergic activity and some direct relaxant activity. Cholinergic-like or stimulatory effects were completely absent. Essentially the same results were obtained with the isolated colon of the various species.

2. In the anesthetized dog, on the other hand, with or without cervical vagotomy, reserpine elicited a stimulation of the small intestine. In dogs with a cervical vagotomy, hexamethonium in an intravenous dose of 2 mgm./kgm. decreased the stimulation evoked by reserpine.

3. In the anesthetized dog subjected to both a transection of the spinal cord at C-6 and a cervical vagotomy, reserpine caused a stimulation of the small intestine which was largely inhibited by the administration of hexamethonium in a dose of 2 mgm./kgm. intravenously.

4. A mechanism has been suggested to explain the stimulation of the small intestine evoked by reserpine; an action on the parasympathetic ganglia which augments the effect of a reduced central sympathetic inhibitory influence. Increased intestinal and colonic activity is the most likely cause of the diarrhea caused by reserpine in certain animals.

REFERENCES

1. Anderson, F., Barrett, W. E., Craver, B., Arch. Internat. de Pharmacodyn. et de Therap. 77:544, 1949.

2. Barrett, W. E., Rutledge, R. A., Rogie, B., Fed. Proc. 13: 334, March, 1954.

3. Bein, H. J., Experientia 9: 107, 1953.

4. Bein, H. J., Annals N. Y. Acad. Sci. 61: 4, April 15, 1955.

5. Muller, J. M., Schlittler, E. and Bein, H. J., Experientia 8: 338, 1952.

6. Plummer, A. J., Barrett, W. E., Wagle, G. and Yonkman, F. F., Fed. Proc. 12: 357, 1953

7. Plummer, A. J., Earl, A., Schneider, J. A., Trapold, J. and Barrett, W., Annals N. Y. Acad. Sci. Vol. 59, Article 1, pg. 8, April 30, 1954.

8. Plummer, A. J., Barrett, W. E., Rutledge, R. and Yonkman, F. F., J. Pharmacol. & Exper. Therap. 108: 292, 1953.

9. Schneider, J. A., Plummer, A. J., Earl, A. E. and Gaunt, R., Annals N. Y. Acad. Sci. 61: 17, April 15, 1955.

10. Trapold, J., Plummer, A. J., Yonkman, F. F., J. Pharmacol. & Exper. Therap. 110: 205, February, 1954.

TREVIDAL, A NEW ANTACID COMPOSITION

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AND EDGAR A. FERGUSON, JR., C. R. T. New York, N. Y.

REMEDIES FOR ulcer and ulcer-like syndrome fall into the categories of:

(1) antacid,
(2) antispasmodics, (1)
(3) ganglionic blocking agents,
(4) surgery.

The oldest and safest is the antacid. While many of the other modalities have received a great deal of scientific attention, the fact remains that antacids have enjoyed a wider spread and more common usage than any other method of treatment. This is by reason of their popular use and because antacids are most often used as an initial treatment. No matter how severe the syndrome may be the antacid should usually be tried first. The reason for this is:

(1) safety,

The antacid combination used in this study was supplied by Organon, Inc., Orange, New Jersey, under the name *Trevidal*.

(2) effectivity over a wide range of conditions,

(3) it is one of the simplest remedies for pain caused by irritation from hyperacidity,

(4) the rapid demonstration of effectiveness pleases the patient and aids in diagnosis.

All treatments now recommended for ulcer and ulcer-like syndromes are symptomatic. It can be shown that whether one uses the antacid, the antispasmodic, (1) the ganglionic blocking agent, or surgery the cause of the condition is not being treated. Each of these methods treat some one outstanding feature of the ulcer syndrome. More fundamental medications, looking toward the cause of the difficulty, take too much time to accomplish the necessary relief from discomfort and pain. Should the origin of the dyscrasia be psychosomatic (2,3) causes, it is necessary to give symptomatic treatment while attempting to re-educate the psyche. Should there be vasomotor imbalance resulting in the phenomena of vague abdominal and gastric distress, long term treatments with sympathomimetic (4) drugs sometimes result in more permanent correction. However, during treatment it is necessary to alleviate symptoms. Should the cause be basically one of arteriosclerotic vascular change (5) it is obvious that long term treatment is most necessary (6).

Treatment of the main causes of ulcer or ulcer-like syndrome directed toward 1) psychic, 2) vasomotor, or 3) vascular rationale has not been signally successful, and each requires long term treatment and a high degree of patient co-operation.

The physician is then left with the great common denominator of treatment for ulcer and ulcer-like syndrome, the antacid. The fact that this remedy is also popular for self-treatment in no way detracts from its importance. While scientific works tend to stress antispasmodics, ganglionic blocking agents, and surgery, because these are of more dramatic interest, the great number of simpler cases must not be overlooked, left to self-treatment (7), nor overtreated.

A new and highly efficient antacid composition has been developed which consists of, in combination, magnesium trisilicate (150 mg.), aluminum hydroxide gel, dried (90 mg.), calcium carbonate (105 mg.), magnesium carbonate (60 mg.), together with a special protein binder derived from oats, and a vegetable gum. The dose is 4 to 12 tablets per day. In our groups 4 tablets were given three times per day.

Out of a group of one-hundred cases forty were selected for exhaustive study of symptomatology before and after treatment. X-ray examination was made before and after treatment where indicated and searching history was elicited from each patient. There were 2 groups. In one group the average age was 42.6 years; and in the other 52.1 years. The average weight of one group was 138.2 pounds; and the other, 160.4 pounds. The number of males and females was approximately equal.

The procedure used included an evaluation of the degree of pain and epigastric distress, the degree of abdominal pain and discomfort, the amount of belching, flatulence, and nausea. A note was made of the degree of flatulence (1), nausea, and the degree of appetite. In addition the number of bowel movements per day (8), before and after treatment, was tabulated. The average patient had complaints which dated back at least 2 years. All the cases had an ulcer-like syndrome which was associated with acute gastritis in many cases. There were a few showing spastic colon, irritable bowel, or hypermotility. In about 25% of the group duodenal ulcer could be proved by x-ray examination. Colitis, visceroptosis, and diverticulitis were associated complaints in a minor number of patients.

A rating scale was made and utilized before and after treatment in each case. The rating scale was as follows:

0 — Symptom not present

1 — Symptom present

2 — Interfered with work and sleep

3 — Extreme discomfort or pain

The epigastric pain was present to a point where it had begun to interfere with work and sleep, approximately 1.5 clinical units. After treatment with Trevidal this degree of pain was greatly reduced to approximately one-half of this rating, 0.8 clinical units. This relief of pain was the cardinal point in the success of Trevidal treatment.

Epigastric distress was evaluated at about 2 clinical units showing that in most cases it interfered with work and sleep. After treatment with Trevidal epigastric distress was reduced to approximately 1, that is, to a point where it was present but did not interfere with work and sleep.

The same rating scale was used for abdominal discomfort and abdominal pain. The abdominal discomfort averaged about one and one-half clinical units, that is, a significant degree of discomfort. This was reduced to about one-half its intensity after treatment with Trevidal.

A similar reaction was shown to pain which averaged about 0.7 clinical units but was reduced to a very low point after treatment with Trevidal. This reaction to abdominal pain after treatment with Trevidal confirms the relief of pain by antacid treatment. In many cases which do not need the additional treatment with antispasmodics, ganglionic blocking agents, or surgery, the antacid constituted the complete treatment.

The degree of belching and flatulence was significantly reduced. Nausea and appetite were also significantly aided by treatment with Trevidal.

The number of bowel movements per day was reduced in cases of hypermotility of the bowel.

In summary it is shown that the major measurable symptoms of the syndrome of ulcer and ulcer-like conditions are the following:

Epigastric distress and epigastric pain

Abdominal discomfort and abdominal pain

Belching and flatulence

Nausea and loss of appetite

Increased number of bowel movements

In the groups tested each case had more than two of these signs and symptoms and, in almost every case, there was some relief after the use of Trevidal.

The symptom of epigastric distress is quite common in the ulcer syndrome. It usually occurs between meals, beginning soon after the meal has started to leave the stomach. It is at this point that acid production continues whereas the amount of food in the stomach has insufficient neutralizing effect. The normal stomach will cease production of hydrochloric acid at this point, but irritation acts as a continuing stimulant to the production of acid.

Most cases, exhibiting epigastric distress, will have pain from time to time. This pain is due to a greater degree of gastric acidity based upon the same mechanism involved in the exhibition of epigastric distress.

Abdominal discomfort, extending throughout the abdomen was present in about half the total number of cases. Generalized abdominal discomfort is characteristic when there are pain and stress areas in the gastrointestinal system. The vegetative nervous system is often responsible for vasomotor changes centering in the abdomen and causing peculiar characteristic sensations all of which have been described as the syndrome of "vague abdominal distress" (4,6). When the ulcer-like syndrome is controlled by the use of Trevidal many of these symptoms disappear completely. While abdominal discomfort was not present to the same degree as abdominal pain or epigastric pain and distress, it nevertheless forms one of the nagging and most persistent of the symptoms which constantly irritate the ulcer victim. This establishes a cycle, increasing the degree of nervousness markedly, which in turn increases gastrointestinal sensitivity, causing greater ulcer-like symptoms.

Generalized abdominal pain, not centered in any particular portion of the abdomen, is usually found in exacerbation of the syndrome. About one-fourth of the patients exhibited pain in some part of the abdomen which could not be localized. When the condition in the gastric and duodenal region was improved there usually was a reduction in the degree of this type of abdominal pain.

Belching and flatulence are present in most cases as a result of irritation within the gastrointestinal system. This is usually due to reflex swallowing of air when pain, discomfort, or distress is present in the gastric tract. Therefore this type of irritation may be generally regarded as a sign of gastric hyperacidity. Most patients experienced considerable relief in the degree of belching and flatulence following treatment with Trevidal and in many it was decreased to a point where it was considered to be completely relieved.

Nausea was present in approximately half the patients sufferings from the ulcer syndrome. Nausea is usually present secondarily to the irritation caused by hyperacidity. Naturally loss of appetite is an accompanying sign. Both the condition of nausea and loss of appetite were improved by the use of Trevidal in almost every case.

The number of bowel movements per day was reduced by treatment with the antacid preparation. This is an expected result (9) because hypermotility follows the reflex effect of irritation of the gastric tract; and the relief experienced in the gastric and duodenal portion, by the use of Trevidal, was reflected in the bowel.

In conclusion, a review of signs and symptoms in most cases treated with Trevidal shows that in several cases of ulcer and ulcer-like syndrome the treatment reduced the degree of gastric irritability and gastrointestinal sensitivity. This result is explained by the consideration that hyperacidity brings about gastrointestinal irritability and sensitivity with its consequent syndrome consisting of the many signs and symptoms usually associated with ulcer. Generally, milder cases are subject to extensive relief; while in the more severe nonsurgical group the treatment generally controls a major portion of the symptoms. This control allows a time for fundamental therapies to be instituted for more permanent relief, when possible.

REFERENCES

1. Kramer, P., Ingelfinger, F. J., Use of Antispasmodics and Spasmodics in the Treatment of Gastrointestinal Disorders, Medical Clinics of North America, 32:1227 (1948).

2. Ingelfinger, F. J., Treatment of the "Irritable" Stomach and the "Irritable" Colon. Medical Clinics of North America, Boston Number: (Sept. 1943).

3. Ingelfinger, F. J., and Abbot, W. O., Intubation, Studies of the Human Small Intestine; The Diagnostic Significance of Motor Disturbance, American Journal of Digestive Diseases, 7:468 (1940).

4. Feinblatt, T. M., Ferguson, E. A., CCK Treatment for the Syndrome of Vague Abdominal Distress, Symptomatic and Roentgenographic Study, American Journal of Digestive Diseases, Vol. 20, No. 8: 242-244, (Aug. 1953).

5. Beckman, H., Pharmacology in Clinical Practice, W. B. Saunders Co., Phila., Pa., p 205 (1952).

6. Feinblatt, T. M., Feinblatt, H. M., Ferguson, E. A.; Treatment of Arteriosclerosis and Vague Abdominal Distress with Niacinamide Hydroiodide (Without Side-Effects), Amer. Jour. Dig. Dis., Vol. 22, No. 1: pp. 5-6 (Jan. 1955).

7. Edlen, A., Pathophysiology of Peptic Ulcer. Supplementum to Acta Medica Scandinavica (1947).

8. Miller, T. G., The Causes of Indigestion and Their Recognition, New England Journal of Medicine, 224:537 (1941).

9. Feinblatt, H. M., and Ferguson, E. A., Gastragogue Effect of Allyl-Bromide Mixture, American Journal of Digestive Diseases, Vol. 13, No. 12:386-390 (1946).

BILIARY DYSSYNERGIA: REPORT OF TWO CASES

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BILIARY dyssynergia, also called biliary dyskinesia, may be defined for the purpose of this report as the occurrence of unusual or abnormal reactions on the part of the contractile elements of the extrahepatic biliary tract resulting in discomfort to the patient. No attempt will be made at systemic description or classification of the forms of dyssynergia. The purpose of this report is to stimulate interest in dyssynergia by the clinical history of two operatively treated cases. This seems to be warranted because clinicians of wide experience at times question the existence of dyssynergia altogether; others, like Cole and Grove (2), do not disclaim its existence but state that it did not occur in their practice. Interest is so much more warranted, because there are patients with considerable pain, as were the two cases to be reported, to whom relief may be offered only if the clinician is acquainted with the syndrome. Some of the fundamental concepts were established by Bergman (1), and by Westphal (2); a great deal of practical work was done in this field by Mirizzi (4) and by Mallett-Guy (3).

CASE REPORTS

Case 1. The patient, a 58 year-old female, came under my observation in February, 1951. She gave the history of cholecystectomy 21 years back, at which time a chronically inflamed gall bladder containing stones was removed. Following this operation for a while the patient had no abdominal complaints; but within half a year an occasional attack of pain occurred, similar to her pre-operative attacks. For years these attacks occurred only rarely but with time, they came more frequently, were accompanied by vomiting, and grew excruciatingly painful. She further stated that for the last three years they were very frequent; for six months prior to examination they occurred almost daily, and she required frequent morphine injections. Because the attacks occurred after meals, she became increasingly afraid to eat and lost a great deal of weight; yet curtailing her diet did not prevent the attacks from recurring. In seeking medical aid, she was examined and treated by various physicians; amongst other diagnostic procedures two gastrointestinal series were made, but these were not relevant. The patient was never jaundiced; there was no history of intestinal bleeding.

The physical examination was not relevant, though it showed that the patient lost a great deal of her optimum weight, weighing at the time of the examination 140 pounds. Stools were consistently negative for occult blood. Chemical examination of the blood including icteric index, Van den Bergh, bilirubin and prothrombin time showed normal values. The crucial question was whether the patient had any somatic pathology that would be amenable to surgical treatment, or did she fall into the psychic class or outright into the drug addict class. There were no positive criteria to rely on for recommending specific therapy, other than the patient's

Fig. 1.

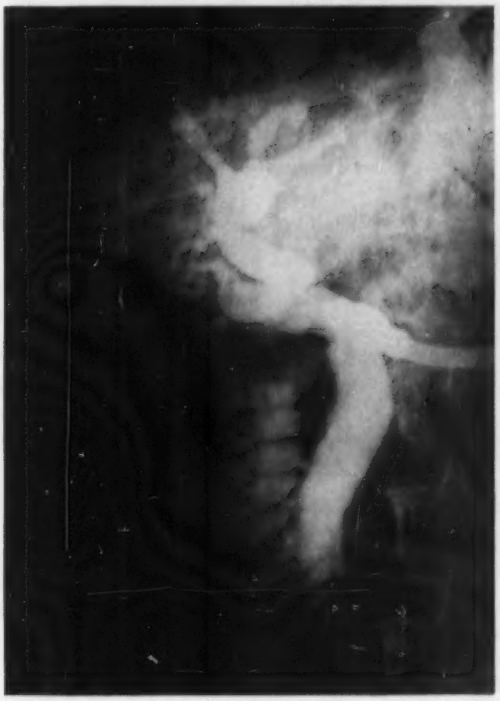


Fig. 2. The width of the duodenum visualized may be used to judge the width to which the common duct is dilated.

personality, the manner in which she presented her complaints, and actual observation of some of the attacks. The patient was advised that there was no definite diagnosis; but laparotomy was proposed with the possible diagnosis of either incomplete small intestinal obstruction, or biliary dyskinesia.

She was explored on Feb. 23, 1951, at the St. Elizabeth Hospital, Elizabeth, N. J. No change was found in the small intestinal tract that would have explained her attacks. The common duct was exposed by the technic used in secondary biliary tract operations: separating all adhesions from underneath the lower surface of the right lobe of the liver until reaching the common duct. This was wider than normal, but no stones were palpated in it, and there were no inflammatory changes observed. The pancreas felt normal. No unusual change was found in the liver. An operative cholangiogram was done (Fig. 1 and 2). This showed that the common bile duct, the common hepatic duct, and the intrahepatic biliary radicals were markedly dilated without the suggestion of stone or of stricture along the course of the ducts; the exit of the contrast material into the duodenum was markedly delayed. The findings of the cholangiogram led to the diagnosis of biliary dyskinesia. The diagnosis having been made, an external choledochoduodenostomy with about a 2 cm. long anastomosis between the common duct and the duodenum was done. Such an anastomosis permits easy escape of the bile into the duodenum and the common duct does not distend anymore when bile is excreted from the biliary passages towards the intestinal tract.

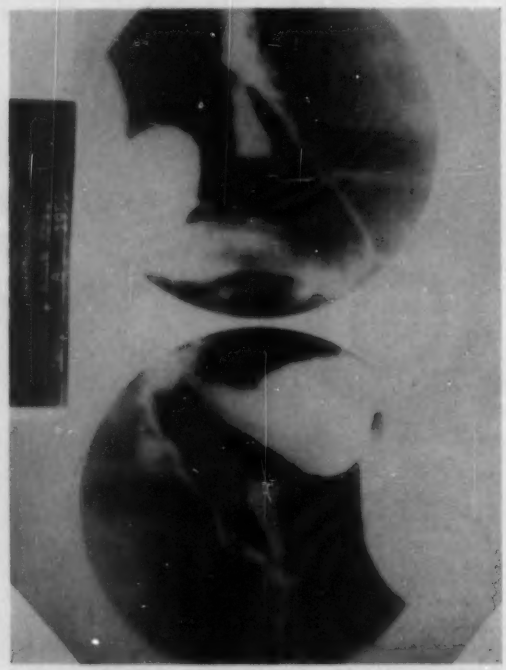


Fig. 3. Spot films taken Jan. 8, 1955, show the prepyloric region of the stomach, the duodenal cap, and the partially filled second and third section of the duodenum; also about an inch long section of the common duct joining the duodenum at the papilla. Note that this section of the common duct is well outlined and near normal in caliber.

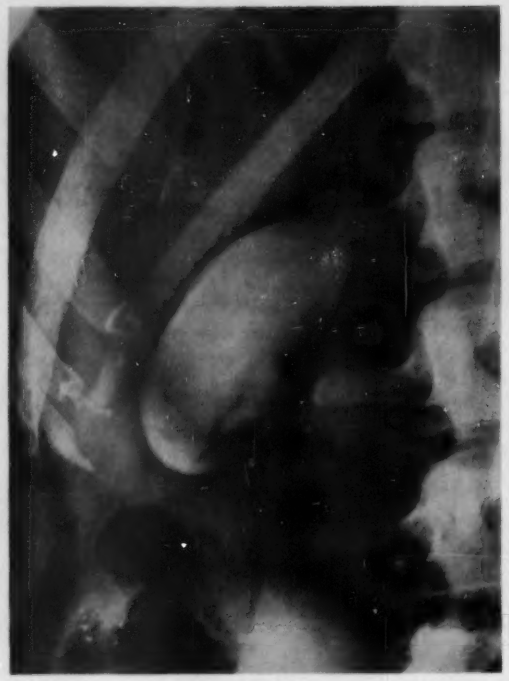


Fig. 4A

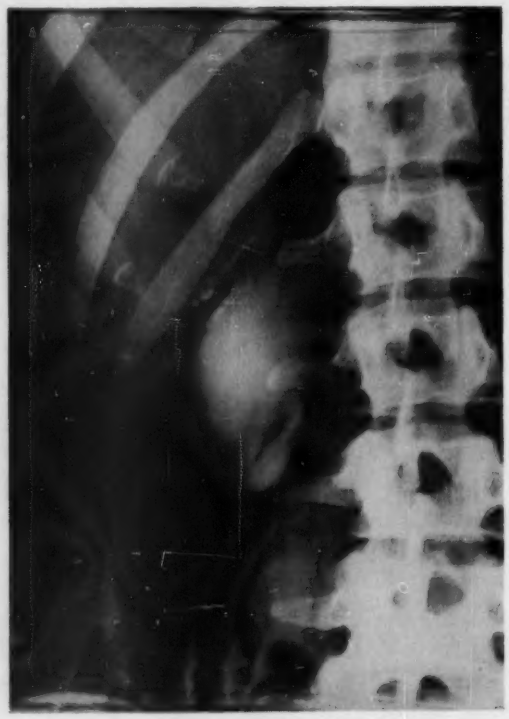


Fig. 4B

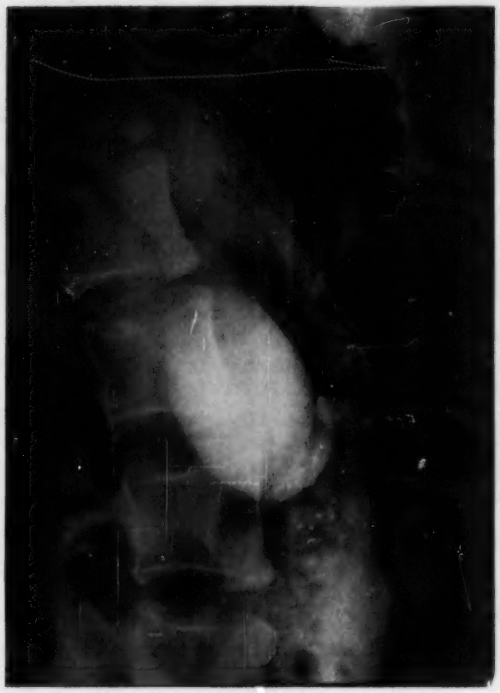


Fig. 5A

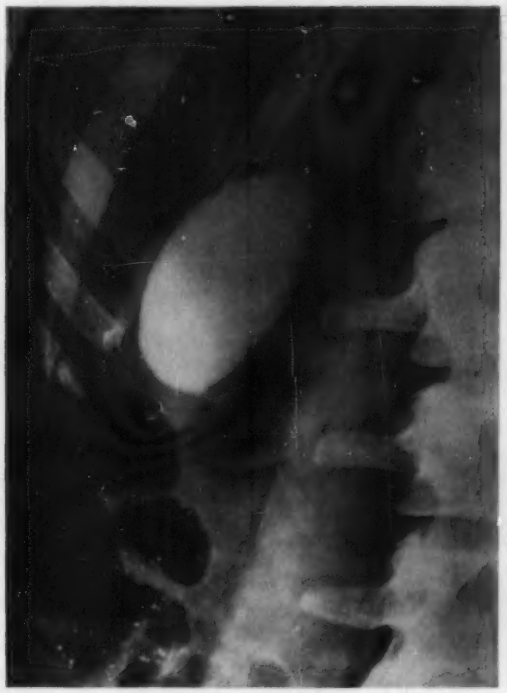


Fig. 5C

Fig. 5B

The patient made an uneventful recovery and left the hospital on the ninth postoperative day. Except for a few days after operation, no analgesics were asked for or needed. The preoperative attacks ceased entirely. She was last re-examined on January 8, 1955. The examination disclosed, that she is free of abdominal distress; that she has a good appetite, that she has regular bowel movements, and that she gained 30 pounds of weight since she was operated upon. Films (Fig. 3) obtained by oral introduction of barium suspension show that a wide communication corresponding to the choledochoduodenostomy is present; barium enters by way of the anastomosis with the common duct.

Case 2. A 25-year old female patient was first seen on Feb. 7, 1950. There was nothing in her previous history pertinent to her complaints which had troubled her for a period of 2 years. They consisted in a bloating feeling in the epigastrium, followed by the feeling of a lump in the right upper quadrant. They occurred postprandially. More recently she also felt a drawing feeling in both inguinal regions, particularly when sitting down. Infrequently she had marked pain in the right upper quadrant. She noticed that canned vegetable soup and chocolate caused discomfort. Physical examination disclosed a movable right kidney; otherwise it was not contributory. Comprehensive investigation was declined by the patient. She was placed on a low fat diet; caroid with bile salts was ordered. Her next examination was on March 13, 1953. By this time her complaints increased in intensity, in duration, and in frequency. Nothing additional was disclosed by physical examination. A gastrointestinal series, a gastric analysis and a sigmoidoscopy were done, but they were not contributory. Radiologic

examination of the gall bladder by Telepaque showed that the gall bladder opacified well; some of the films showed a somewhat irregular radiotranslucent line starting at the gall bladder fundus and extending half way up the gall bladder shadow (Figs. 4A, 4B); other films showed a radio-opaque whip-like appendage attached to the gall bladder fundus (Figs. 5A, 5B and 5C). Nothing was observed on the radiograms indicating the presence of stones. The patient was advised that there was no definite diagnosis, and that she should be subjected to exploration. She preferred to continue with a medical regime. She returned for examination in December 1954. By this time, she had considerable and frequent pains. Re-examination of the gall bladder by x-ray gave findings similar to those previously established (Fig. 6). She accepted exploration.

She was operated upon on Feb. 3, 1955 at the St. Elizabeth Hospital, Elizabeth, N. J. The abdomen was entered with a right, upper, paramedian incision. Numerous filmy adhesions were found between the gall bladder and the duodenum. A somewhat obliquely running, fibrous, strand-like structure was seen in the gall bladder wall near to the gall bladder fundus. No stones were palpated. A Lindeman needle was inserted into the gall bladder, its intraluminal position verified by the recurrent bile flow. The needle was connected by way of tubing to a spinal manometer and to a syringe; sterile water was injected into the gall bladder. At this time the strand like structure produced a definite inward fold on the gall bladder. The emptying pressure of the gall bladder was measured as being in excess of 600 mm. of water; the water flowed back and out at the top of the manometer, which was 600 mm. high. Then cholangiograms were done with the needle in the same position and with diodrast (Fig. 6). The cholangiograms did not show any irregularity of the biliary tract; notably, the common duct was well outlined, its caliber at its maximum distention was within normal limits, and contrast material emptied into the duodenum easily; there were no areas indicative of stone, dilatation, or stricture. Cholecystectomy was done with individual ligation of the cystic duct and of two almost equally developed cystic arteries. Routine appendectomy was done; the abdomen was closed.

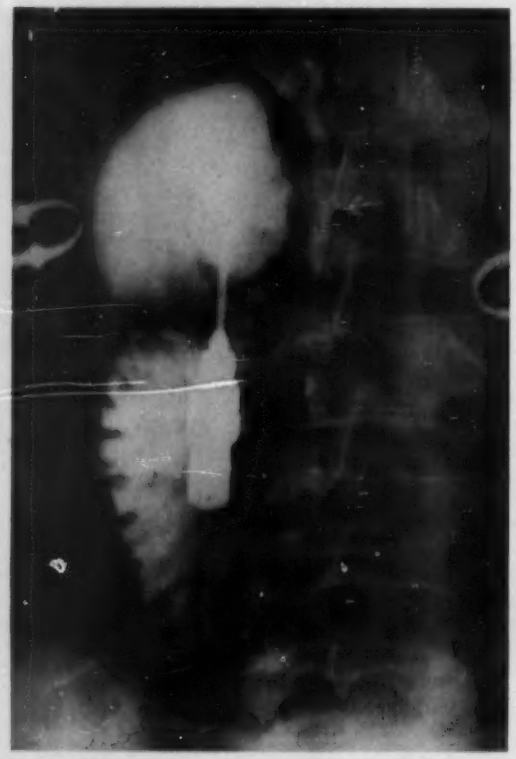


Fig. 6. Arrow points to the common hepatic duct. It is of normal caliber. The contrast material filling can be followed into the right and into the left hepatic duct.

The gall bladder with the attached cystic duct was immediately opened to observe any obstruction in the cystic duct. None was found. The gall bladder fundus was markedly thickened. In this thick part a 3 mm. wide aperture was found. The pathologic report was: gross, 1/chronic cholecystitis, 2/diverticulum at the fundus; microscopic, 1/gall bladder wall: chronic cholecystitis, 2/fundus of gall bladder at diverticulum: chronic cholecystitis.

The postoperative course was uneventful. The patient now, 5 months after the operation, has no abdominal complaints. Although preoperatively, she was afraid to eat, now she has a good appetite and she eats without discomfort.

DISCUSSION

Both of the reported cases were subjected to laparotomy without definite diagnosis. The operative cholangiogram, for which preoperative arrangements were made, disclosed in the first case a marked dilatation of all of the extrahepatic biliary ducts and some of the intrahepatic biliary ducts, but no stones. It is debatable whether there was or was not an organic stenosis present. The patient was never jaundiced, her blood chemistry did not show an elevation of the blood bilirubin, and the pain occurred in attacks. These points suggest that the obstruction occurred intermittently and, therefore, was not organic. This means that there was an intermittent spasm of the sphincter of Oddi. The treatment may have been an endocholedochal or a transduodenal papillotomy. The common duct was dilated. A side-to-side anastomosis between the dilated common duct and the duodenum could be done without difficulty and a large stoma made. Therefore this method seemed to be desirable in this case. The roentgenograms done about 4 years after the operation show that the anastomosis is wide open and affords ample drainage.

Chronic cholecystitis and gall bladder diverticulum were found in the second case by the pathologist. A patient who has chronic cholecystitis without stones usually does not improve by cholecystectomy. Yet, cholecystectomy, in this case, promised to give relief, because the emptying pressure of the gall bladder was much higher than normal: i.e. instead of being 300 mm. water or less, it was in excess of 600 mm. Normal caliber of the common duct and prompt emptying of contrast material from duct into duodenum eliminated the common duct as the site of the difficulty. These data,

in conjunction with the pressure determination, localized the site of the difficulty in the cystic duct. No organic change was found there. The conclusion was that there was an intermittent spasm of some section of the cystic duct present, probably at the so-called collum-cysticus sphincter.

SUMMARY

Two cases are reported. The pathology in both belongs to the group of dyssynergia. There was no definite diagnosis before either operation. Both cases called for laparotomy. In the first case, cholangiogram was done during the operation; this led to diagnosis and indicated proper treatment. In the second case, cholangiogram was not enough; determination of the emptying pressure of the gall bladder was necessary; the conjunction of both measures suggested the correct therapy.

This report only serves to stimulate interest. The nature and the classification of dyssynergia are not discussed. For such information the reader is referred to the quoted literature.

REFERENCES

1. von Bergmann: Funktionelle Pathologie. Julius Springer, Berlin, 1931.
2. Cole, H., and W. J. Grove: Persistence of Symptoms following Cholecystectomy with Special Reference to Anomalies at the Ampulla of Vater. Ann. Surg., 136, 73-82, July 1952.
3. Mallett-Guy, P.: La Chirurgie Biliaire. Masson & Cie, Paris, 1947.
4. Mirizzi, P. L.: Operative Cholangiography: Its contribution to the Physio-Pathology of the Common Bile Duct. Lancet 2, 366, (Aug. 13) 1938.
5. Westphal, Gleichmann und Mann: Gallenwegefunktion und Gallensteinleiden. Julius Springer, Berlin, 1931.

ABSTRACTS ON NUTRITION

GRIEP, A. H.: *Insulin edema: report of a case.* J. Indiana State Med. Assn., 48, 8, August 1955, 872.

The case is reported on a nurse who developed severe general anasarca from the use of insulin (N.P.H.). Such cases are rare but others have been reported. Diuresis was produced by reducing salt and using diuretics, so that the edema disappeared in a week, and has not returned despite the fact that treatment was continued with the same kind of insulin. There was no skin reaction to the intradermal injection of crystalline insulin. It is possible that Benadryl or other antihistamines might have been of benefit.

JACKSON, W. P. U.: *Ocular nerve palsy with severe headache in diabetes.* Brit. Med. J., Aug. 13, 1955, 408.

Jackson, working in the Diabetic Clinic of the University of Capetown, South Africa, describes 4 diabetic patients, of whom 3 were negroes, and in all of whom very severe hemicrania was associated with paralysis of the 3rd and/or 6th cranial nerve. In all cases the pain and paralysis eventually and spontaneously disappeared. All of the cases were poorly controlled. It is not too uncommon to encounter ocular palsies in diabetics but the association of severe one-sided head pain with such paralysis has not before been described. Jackson feels that the syndrome is a manifestation of diabetes mellitus,—one more form of diabetic neuropathy.

BEST, C. H., HARTROFT, W. S., LUCAS, C. C. AND RIDOUT, J. A.: *Effects of dietary protein, lipotropic factors, and re-alimentation on total hepatic lipids and their distribution.* Brit. Med. J., June 18, 1955, 1439.

In rats fed diets containing a moderate amount of fat and 9 percent or less of protein, supplementary choline failed to prevent completely the accumulation of fat in the periportal regions of the liver. Lack of adequate protein resulted in the appearance of fat in the periportal areas, while deficiency of choline (or precursors) caused an accumulation of fat in the cells bordering on the central vein. When rats were transferred to an adequate diet (containing 18 percent casein and 0.5 percent choline chloride) after a period on a low protein ration (3% casein), there was a dramatic appearance of a transient fatty liver (total lipids 18 percent), the fat appearing in periportal positions only. During 3 weeks on the same ration the hepatic lipids returned to normal. Other rats pair-fed the same amounts of a commercial ration did not develop fatty livers, so that the transient appearance of periportal fat is not entirely due to the increased food intake. The authors feel that the clinical use of choline and methionine to repair the liver damage produced by multiple deficiencies—that is, of protein, minerals, vitamins, etc.—is doomed to failure because most hospital diets supply an abundance of lipotropic factors. In rats on a low-fat, low-protein, low-choline diet, the liver microscopically may closely resemble what is seen in Kwashiorkor.

PORTEOUS, V. M.: *Diabetes mellitus with Addison's disease.* New Zealand Med. J., 54, 299, Feb. 1955, 18.

A case of co-existent diabetes mellitus and Addison's disease is described. Addison's disease developed very insidiously and eventually resulted in decreased insulin requirements. Cortisone therapy (25 mg. daily) resulted in an abrupt increase in insulin requirements and in marked clinical improvement.

FRENCH, D. G. AND ISRAELS, M. C. G.: *Discussion on anemia in general practice.* Proc. Royal Soc. Med., 48, 5, May 1955, 347.

Iron-deficiency anemia is by far the commonest form of anemia seen in general practice. Pernicious anemia, the leukemias, aplastic anemia and other rare forms of anemia such as non-tropical sprue, form a small per-

centage. When pernicious anemia is suspected the case should be sent to the hospital for an accurate diagnosis, since the use of vitamin B_{12} may make a diagnosis practically impossible. The authors like to use iron intravenously (Ferrevenin) since the results are so good and reactions can be avoided by giving the drug slowly.

DARBY, W. J.: *What lies ahead in the field of nutrition?* Ill. Med. J., 107, 6, June 1955, 311.

Darby expands upon several currently promising fields of nutritional investigation, such as pyridoxine deficiency; the interrelationships among vitamin B_{12}, folic acid and ascorbic acid; the possibility of isolating the intrinsic factor as a therapeutic agent; the relationship of pyridoxine deficiency to atherosclerosis; sodium chloride in hypertension; the role of trace elements; the wide-spread nature of iodine deficient goiter (the commonest dietary deficiency in the world); the control of pellagra by enrichment of cereals; and the use of vitamin B_{12} following gastrectomy.

SCHROEDER, H. A.: *Is atherosclerosis a conditioned pyridoxal deficiency?* Jour. Chronic Dis., 2, 1, July 1955, 28.

Since atherosclerosis has been produced in monkeys and hypertension in the rat by deficiency of vit. B_6, there is the possibility that human atherosclerosis and/or hypertension is influenced by pyridoxine deficiency. The American diet appears to be marginal in B_6 with reference to some cooked and processed foods. The human body contains many "abnormal" trace elements, several of which could compete for an essential metal in a pyridoxal-enzyme system and reduce the amount available for metabolism, thus producing a conditioned deficiency. There is no experimental evidence against the hypothesis of the author. Proof or disproof awaits facts backed by clinical experiments.

ANTIA, F. P. AND COOPER, S. H.: *Chronic rectal bleeding due to milk.* Brit. Med. J., June 11, 1955, 1416.

An unusual case is described of a woman aged 38 in India who bled from the rectum every day for 7 years. Punctate bleeding all over the colon was found and allergy to milk was suspected. All food was withheld except fruit juice and water, and for the first time in 7 years the bleeding stopped. When milk was permitted, bleeding began again. The patient was then desensitized to milk by gradually increasing the amount consumed by one drop per day.

WOLFF, O. H. AND MADDISON, T. G.: *Insulin zinc suspension in childhood diabetes.* Brit. Med. J., Aug. 13, 1955, 413.

The authors obtained good control in 20 cases of juvenile diabetes mellitus by the use of insulin zinc suspension (I.Z.S.). The mixture used contained 3 parts amorphous to 7 parts of crystalline zinc suspension. The amount and distribution of carbohydrate between the various meals was regulated according to the child's appetite and the urine blood sugar levels. The ratio of carbohydrate taken at breakfast, mid-morning snack and dinner to that taken later in the day was usually 3:2. (N.B. In England, "dinner" is the noon meal and there follows "tea" and "supper.")

NOTICE

Beginning with the January 1956 issue, The American Journal of Digestive Diseases will be published by Paul B. Hoeber, Inc., 49 East 33rd Street, New York 16, N. Y. The journal has been purchased from the Sandfield Publishing Company. Authors should send all manuscripts directly to Mr. Hoeber who will submit them to his Editorial Board, prior to publication. All subscriptions should also be sent directly to Paul B. Hoeber, Inc., at the above address.

Owing to Mr. Hoeber's eminence in the field of medical publication, we are certain that The American Journal of Digestive Diseases will enjoy a bright future.

Sandfield Publishing Company

EDITORIAL

AN EDITOR RESTS HIS CASE

I asked to be relieved of the Editorship of this Journal because of the increasing responsibilities of my own practice of medicine. Partly on this account, but also for other reasons, the Sandfield Publishing Company entered into negotiations with Mr. Paul B. Hoeber of New York for the sale of the Journal. The transaction has been completed and, beginning with the January 1956 issue, the Journal will henceforth be published by a veteran in the field of medical publications — Paul B. Hoeber, Inc. (Medical Book Department of Harper and Brothers, 49 East 33rd Street, New York 16, N. Y.).

I believe that Mr. Hoeber, with the assistance of a select Editorial Board, will find it possible to carry this Journal to a degree of perfection which it has never before manifested. I am particularly glad, inasmuch as I was one of the founders (with Frank Smithies) of the Journal in 1934. For that reason, I call upon the many authors who have sent us contributions in the past 21 years to continue to support the Journal. As for the subscribers, I can assure them of complete satisfaction under the new set-up.

Beaumont S. Cornell, M. D., F.A.C.P.
Editor.

BOOK REVIEW

PEPTIC ULCER: DIAGNOSIS AND TREATMENT. Clifford J. Barborka, M. D. and E. Clinton Texter, M. D. Little, Brown and Company, Boston. 1955. $7.00.

This book, which runs to about 300 pages, is meant primarily for physicians, but most of it would be more or less intelligible to patients. The one striking feature of the volume is the fact that the authors apparently have no pet theories, no panaceas, and not too optimistic an outlook for persons afflicted with this recurring disease. Another excellent feature is their handling of the dietary problems. The various types of medical and surgical treatment are fully covered in a critical way. We feel that any physician studying this book will finally know all he needs to know about peptic ulcer. We highly recommend it.

GENERAL ABSTRACTS OF CURRENT LITERATURE

OLIVER-PASCUAL, E., SANZ-IBANEZ, J., ANDOLZ, F., ELOSEGIN, C., OLIVER, A., ELEICEGUI, J. AND CASTILLO, E.: *Idiopathic ulcerative colitis with pernicious (Biermer-Addison) anemia and duodenal pseudo-ulcer with multiple nutritional deficiencies.* Rev. Espanola d.l. Enferm. d. Apparado dig. y.d.l. Nutrit., XIV, 2, March-April 1955, 163.

The authors describe a case of multiple nutritional deficiencies of subclinical type, whose symptoms were caused by a viral infection which gave rise to ulcerative colitis and duodenitis. The latter was accompanied by periduodenitis and viral mesenteric lymphadenitis. The nutritional deficiencies plus the viral infection, plus natural predisposition, caused true pernicious anemia with severe megaloblastic bone-marrow and also hepatitis. A diet rich in protein and the use of vitamin B_{12} brought about a clinical cure of the anemia and diarrhea, so that the lesions of the ulcerative colitis became latent.

GONZALES, J. M.: *Operative results in 59 cases of Crohn's disease.* Rev. Espanola d.l. Enferm. d. Apparado dig. y.d.l. Nutrit., XIV, 2, March-April 1955, 145.

Prognosis in Crohn's disease depends on careful anatomical and histological examination of diseased tissues. He has followed his cases for 5 years. Exclusion operations are superior to resections. In a large number of cases the disease is malignant, a fact which only appears after a long follow-up.

HILL, J. R.: *Diseases of the terminal portion of the colon.* J. Indiana State Med. Assn., 48, 8, Aug. 1955, 857.

Twelve per cent of all malignant growths of the human body originate in the anus, rectum or lower part of the sigmoid colon. The commonest type of tumor found here is the adenomatous polyp. Ten per cent of persons more than 40 years of age have been found, in various detection centers, to have one or more adenomatous polyps in the lowest 10 inches of the bowel. Detection is facilitated by the fact that 70 per cent of all adenomatous polyps and cancers of the colon can be reached with a 10 inch sigmoidoscope.

LYNCH, R. C., HUTTON, S. B. AND JOHNSON, G. D.: *Carcinoma of the cecum (clinical analysis of 33 cases).* Amer. J. Gastroent., 24, 1, July 1955, 53.

Cancer of the cecum develops at an earlier age in men than in women. A patient with a long history of abdominal pain and with weight loss and anemia should be given a most complete examination. Rectal bleeding and a change in bowel habits are further symptoms emphasizing the same necessity for examination. The earlier the operation, the better the results. Abdominal exploration is justifiable when cecal cancer is suspected, even if the x-ray studies are negative.

BOROS, E.: *Hyperchlorhydria—can it be controlled medically?* Amer. J. Gastroent., 24, 1, July, 61.

Boros found it practically impossible to neutralize completely gastric acidity over an appreciable length of time by the use of food or calcium carbonate in large impossible to tell, by *any* method, just where gastric cancer. In gastritis, a better neutralization could be attained. Boros wonders if ulcer does not cause hypersecretion of acid, rather than the reverse. Many persons with arrested ulcers still have excessive acid secretion.

SILVERMAN, F. N.: *Gastroesophageal incompetence, partial, intrathoracic stomach and vomiting in infancy.* Radiology, 64, 5, May 1955, 664.

The term "chalasia" is used in this article to indicate incompetence of the cardia. It is not difficult to demonstrate reflux of gastric contents into the esophagus in those cases in which it occurs, but it is often impossible to tell, by *any* method, just where gastric mucosa ends and esophageal mucosa begins. For that reason, differentiation between "chalasia" and partial thoracic stomach is not always possible. The two conditions may be identical. In some cases followed by x-ray over a number of years, short esophagus appeared to develop and, hence, it is thought that short esopha-

gus is not a congenital abnormality but a result of irritation from regurgitated gastric contents with the production of esophagitis, and subsequent cicatricial contraction. Postural treatment, i.e., keeping the patient in the upright position, is the method of choice, and the only effective method where gastroesophageal incompetence is discovered in early infancy.

ROOT, J. C. AND LEWIS, R. F.: *A comparison of a new cholecystographic medium, Teridax with Telepaque.* Radiology, 64, 5, May 1955, 714.

Teridax was used in 472 patients and the results were compared with those obtained with Telepaque in 426 patients by Dunne, et al., and those obtained with Teridax in 204 cases by Shapiro. Teridax yields visualization of the gall bladder comparable to that achieved by Telepaque, but up to twice as much medium in relation to body weight is required as with Telepaque. This increased dosage is the probable cause of the high incidence of side-effects in the authors' series.

RINEHART, R. E.: *Chloroquine therapy in rheumatoid arthritis.* Northwest Med., 54, 7, July 1955, 713.

Having observed that 95 percent of patients with rheumatoid arthritis harbored *E. histolytica* in their stools, Rinehart employed amebacides, particularly Chloroquine 0.25 gm. twice a day for 3 to 6 weeks. He obtained improvement or complete remissions of arthritis in 8 of 11 children. Eight of 14 adults with rheumatoid arthritis experienced a lesser degree of improvement under similar treatment. Rinehart quotes Haydu to the effect that favorable results may be obtained on smaller doses of Chloroquine (0.25 gm. twice weekly). It is possible that the improvement may be metabolic due to an interference with the action of adenosine triphosphate.

RINEHART, R. E. AND MARCUS, H.: *Incidence of amebiasis in healthy individuals, clinic patients, and those with rheumatoid arthritis.* Northwest Med., 54, 7, July 1955, 708.

The authors found that 30 percent of normal persons living in Oregon are at any one time subclinically infected with *E. histolytica.* A similar incidence is found in persons with a wide variety of illnesses. Nearly all (95 percent) of patients with rheumatoid arthritis are infected with E. histolytica. The only prominent gastrointestinal complaints encountered in the patients in this series were those ordinarily ascribed to irritable bowel and chronic constipation, approximately 50 percent describing one or both. Several workers have previously described patients having both rheumatoid arthritis and amebiasis. They stated that the arthritic symptoms often improved after administration of amebacides.

HARTNETT, B. S.: *Liver damage and eosinophilia following chlorpromazine therapy.* Brit. Med. J., June 18, 1955, 1458.

A depressed patient who was receiving chlorpromazine developed nausea and vomiting after 10 days' therapy, jaundice developed, and he showed a very high eosinophil count (58 per cent). Liver biopsy showed "cholangiolytic hepatitis." At operation a T-tube was placed in the common duct. His convalescence was uneventful. Chlorpromazine was considered to be responsible for his hepatitis and an element of allergy to the drug was considered probable. Some permanent liver damage appears likely.

BURNETT, W.: *Traumatic rupture of the pancreas.* Brit. Med. J., June 18, 1955, 1455.

Symptoms following traumatic rupture of the pancreas may be acute (resembling hemorrhagic pancreatic necrosis) or more insidious. Estimation of blood serum amylase helps in making the diagnosis. A case is described in which the pancreas was transected by trauma in its middle portion. At operation a drainage tube was led out from the site of rupture but no attempt made to repair the pancreas for fear of causing worse trouble. Fluids were restricted, and propantheline bromide was given by mouth to suppress pancreatic secretion. The patient made a good recovery.

ALBOT, G., BASSON, A., FOULET, J. AND CINQUALBRE, C.: *La colicistografia de frente y de perfil, con evacuacion accelerada y minutado.* Rev. Espanola de las Enferm. del apparado dig. y de la Nutricion. XIV, 2, March-April 1955, 119.

The authors describe their method for cholecystography, consisting of simultaneous A-P and lateral films, with accelerated emptying time in minutes. This gives them the gallbladder volume as well as the coefficient of volumetric depletion.

MACLAREN, W. R.; BRUFF, W. C.; EISENBERG, B. C.; WEINER, H., AND MARTIN, W. H.: *A clinical comparison of Carbinoxamine Maleate, Tripelennamine Hydrochloride, and Bromodiphenhydramamine Hydrochloride in treating allergic symptoms.* Ann. Allergy, *13*:307 (May-June) 1955.

Although presently available antihistamines are reasonably efficient in counteracting histamine, complete relief of symptoms does not always follow their use and the numerous side effects, particularly somnolence, impair their usefulness in many patients. The new antihistamine, Clistin ® Maleate (Carbinoxamine Maleate, McNeil) was developed with the aim of overcoming these objections. This antihistamine is compared in clinical effectiveness and incidence of side effects with two previously established antihistamine compounds—bromodiphenhydramine hydrochloride and tripelennamine hydrochloride.

Of the 70 patients in the series, 41 had allergic rhinitis, 26 allergic rhinitis and asthma, 3 allergic rhinitis and eczema.

The amounts by which actual symptoms were reduced were, respectively, tripelennamine hydrochloride 24.3 per cent, carbinoxamine maleate 18.9 per cent, and bromodiphenhydramine hydrochloride 14.3 per cent.

Subjective relief as reported by patients showed order of effectiveness: tripelennamine hydrochloride, bromodiphenhydramine and carbinoxamine maleate.

The number of cases experiencing side effects and the

approximate severity thereof are shown in Table. Sedation was estimated as follows: 1 plus if spontaneously noticed by the patient but causing no difficulty; 2 plus, if conscious effort was required to keep fully alert; and 3 plus, if effort was necessary to keep awake.

NUMBER OF PATIENTS IN GROUP OF SEVENTY SHOWING SIDE EFFECTS FROM TREATMENT WITH ANTIHISTAMINES AND A PLACEBO

Side Effect	*Pyribenzamine*		*Cliatin*		*Ambodryl*		*Placebo*	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent
Sedation one plus	14	20	8	11.4	12	17.2	0	
Sedation two plus	5	7.1	1	1.4	8	11.4	1	1.4
Sedation three plus	4	5.7	2	2.9	2	2.9	0	
(total sedation)	(23)	(32.8)	(11)	(15.7)	(22)	(31.5)	(1)	(1.4)
Dizziness	4	5.7	1	1.4	2	2.9	2	2.9
G. I. distress	4	5.7	3	4.3	4	5.7	3	4.3
Headache	1	1.4	3	4.3	3	4.3	0	
Dryness mouth or nose	1	1.4	0		0		0	
Total all complaints	33	47%	18	25.7%	31	44.4%		8.6%

It is noteworthy that the order of subjective relief is the same as the frequency of producing somnolence. The sedative effect may make patients feel better than their symptom count indicates them to be.

Carbinoxamine maleate produced the fewest complaints of drowsiness as well as the lowest incidence of all side effects of the three antihistamines. Somnolence in particular was encountered only half as often. This suggests that larger doses than the recommended 4 mg. could be used, undoubtedly producing greater symptom control without raising side effects beyond an acceptable level.

FINER, D. I. AND FRY, J.: *Peptic ulcer in general practice.* Brit. Med. J., July 16, 1955, 169.

The authors are general practitioners in London who believe that the general man is in a position to throw some light on the natural history of several diseases—in this case, peptic ulcer. In their two practices, out of 10,000 patients at risk, they had, on July 1, 1954, 177 peptic ulcer cases (gastric 45, duodenal 132). Of these 124 had a history of five or more years' duration. These 124 cases were analyzed. 70 per cent of the patients did not lose any time from work. 25 per cent were operated upon, all with good results. Of the medically treated patients, 30 per cent needed no medical attention. Results were similar in both gastric and duodenal ulcers. Hemorrhage occurred in 18 per cent and perforation in 10 per cent of cases. There was no obvious prevalence of any other associated disease except for neurosis. A fairly severe psychoneurotic state was present in 16 per cent of duodenal and in 7 per cent of gastric ulcer patients. The authors feel that "these results represent a not unsatisfactory economic and personal control of the condition."

COBURN, W. AND BAKER, J. W.: *Leiomyosarcoma of the stomach: a case report.* Bull. Mason Clin., 9, 2, June 1955, 43.

A large leiomyosarcoma was successfully removed from a 65 year old woman. One point of interest was that the patient postponed the operation for 4 years, and yet, in view of the fact that no metastases were found, it appears that she would get a cure. Another point of interest was that, in her consultations with many different doctors, the tumor was not always palpable. She wasted her time mostly with cultists, especially the purveyers of Kock's treatment and the givers of colonic irrigations. Finally, being a Jehovah's Witness, she refused blood transfusion, but would permit Dextran as a substitute.

GORDON, J. D.: *The early operative treatment for gastric hemorrhage.* Am. J. Gastroent., 24, 1, July 1955, 13.

This article is a plea for prompt surgical intervention in cases of gastric hemorrhage which are severe and which promise to exanguinate the patient. The mortality rate in massive bleeding cases is about 20 percent. The mild or moderate bleeders are not surgical problems. In severe cases, surgery should be done during the bleeding phase, and such surgery carries a reasonably low mortality rate. Gordon is not influenced in his decision to operate by the age or sex of the patient. It is the patient who requires tremendous amounts of transfused blood to stabilize his blood counts (from 2,000 to 5,000 cc. per day) who requires surgery. In cases in which the hemorrhage stops, a resumption of hemorrhage may prove fatal even if only 400-500 cc. of blood are lost. The cases forming the author's material were all instances of peptic ulcer.

VELIATH, G. D., RAN, D. S. S. AND SWAMIDASAN, G.: *Portal cirrhosis.* J. Indian Med. Assn., 25, 3, July 1, 1955, 90.

Many factors are involved in the evolution of portal cirrhosis of the liver. In South India malnutrition is an important etiological factor. Fibrosis in these cases follows the same pattern of liver injury, inflammatory cell infiltration, especially around the portal tracts and central veins, capillary formation and eventual condensation into fibrous tissue. Liver injury is brought about

not by toxins or virus but by the mechanical rupture and death of liver cells distended with fat. Alcoholic cirrhosis, where fatty infiltration is a prominent feature, is evidently brought about in a similar manner, the crucial factor being malnutrition usually associated with chronic indulgence in alcohol, and not due to the action of alcohol on the liver cells.

SARIN, L. R., GOYAL, R. K. AND SARIN, J. C.: *Primary carcinoma of the liver.* J. Indian Med. Assn., 25, 3, July 1, 1955, 80.

Primary cancer of the liver is more common in Africans and Orientals. In Western countries the percentage is 0.14 of all autopsies, whereas in Bantu races 90.5 per cent of all malignant diseases are primary carcinoma of the liver. Cirrhosis of the liver is intimately associated with primary hepatic cancer. Neoplastic transformation occurs in 20 to 25 per cent of all cirrhotic livers. Concomitant cirrhosis is largely responsible for ascites, dilated abdominal veins, edema and hematemesis which are so commonly met with in primary liver carcinoma. Malnutrition—particularly the lack of protein and vitamin B complex—is an important cause of cirrhosis, and the disease is more common in men than in women. Diagnosis is best made by needle biopsy.

KRANTZ, J. C.: *Cholinergic blocking agents on the gastrointestinal tract.* Am. J. Gastroent., 24, 1, July 1955, 31.

Krantz, in surveying the effects of the various available blocking agents (atropine, hematropine methylbromide, Trasentin, Pavatrine, Bentyl hydrochloride, and Pamine bromide) feels that atropine benefits more patients for longer periods of time than any of its substitutes. Cholinergic-ganglionic blocking agents, such as Banthine, Pro-Banthine, Antrenyl, Prantal and Monodral should be employed in cases in which atropine or its substitutes are insufficiently effective. From a clinical standpoint, the danger of Banthine-type therapy lies in a false sense of security which it frequently gives the patient. At times drugs of this type will relieve pain when acid and irritation still are present.

HUGHES, E. S. R.: *Stones in the common bile duct: the role of operative cholangiography.* Med. J. Australia, June 4, 1955, 820.

Hughes did 100 operative cholangiograms, 80 of which were done as a routine investigation in the course of cholecystectomy for gallstones. In 3 cases, stones were discovered which otherwise would have been overlooked. The procedure is of little or no trouble to the surgeon and satisfactory films can always be obtained. However, the interpretation of the films is uncertain because of false positives and false negatives. The procedure, if undertaken in conjunction with other evidence of common duct stone, is of real value.

HARE, W. S. C.: *The indications for intravenous choledochography: preliminary report.* Med. J. Australia, June 4, 1955, 823.

Intravenous "Biligrafin" was used, and it was found that the examination is unsatisfactory in cases of impaired liver function. It is concluded that the presence of clinically detectable jaundice or a strongly positive response to the cephalin flocculation test precludes its use. The post-cholecystectomy syndrome is the greatest field for application of the test, provided it is done before liver function is impaired. The test may eventually replace oral cholecystography.

GANDARILLAS, M. P.: *Lymphosarcoma of the stomach.* Arch. Cubanos d. Cancerologia, 14, 4-6, Apr.-June 1955, 238.

A 34 year old woman with lymphosarcoma of the stomach presented a healthy appearance. X-ray examination revealed a tremendous filling defect of both curvatures in the antrum. Four-fifths of the stomach was resected. A huge tumor affecting the inferior third of the stomach was found. The wall at this point was 3 cms. in diameter. Microscopic examination showed a polymorphous histological structure in different parts of the tumor and in the metastatic lymph nodes.

MCBURNEY, R. P.: *Surgical treatment of pancreatic disease.* Amer. Pract. & Dig. Treat., 6, 8, Aug. 1955, 1221.

McBurney stresses the inaccessibility of the pancreas and our paucity of knowledge with respect to the etiology of diabetes, and the fact that only in recent years have we recognized chronic relapsing pancreatitis. In acute pancreatitis, the diagnosis can scarcely be made without a blood amylase determination made early in the disease. If the diagnosis can be made, surgery is avoided and reliance placed on antibiotics and electrolytes. When there is doubt about the diagnosis operation may have to be undertaken and if pancreatitis is found, the operation will depend on its severity. If severe, drainage only is attempted, otherwise the gallbladder (with stones) is removed and a T tube placed in the common duct. In chronic recurring pancreatitis, attention may have to be directed to the gallbladder. If pseudocysts are present, cystenterostomy is the operation of choice. In the case of cancer of the pancreas, the operation of pancreatoduodenotomy may be performed but five-year survivors from this operation are few in number. The diagnosis of islet cell tumor depends on fulfilling Whipple's triad of symptoms. The tumor cannot always be found on laparotomy, in which case the body and tail are removed for pathological examination. If the tumor is not present in the specimen, the head of the pancreas may then have to be removed later. Usually, however, the insuloma can be detected at operation and removed.

HUNGARIAN NURSE TELLS OF HIGH MORTALITY AMONG PREMATURE BABIES

Inadequate care given premature babies and other hospital patients under the Communist regime in Hungary was described in a recent broadcast over the U.S. Information Agency's Voice of America.

A trained nurse who fled to the West said in an interview recorded in Europe that despite 17 years experience she finally reached the point where she could no longer tolerate conditions in the large general hospital in Budapest where she was employed.

Six premature infants are usually crowded into incubators meant only for four, she said, adding:

"The doctors and nurses do all they can for the babies. But what can they do when one nurse has to take care of 18, 20, often 23 premature babies at one time?"

It is on the nurse's work that the lives of these babies largely depend, she said, and the mortality rate among the infants is high.

The overload of work and the impossibility of doing her job properly led to her decision to escape from Communist Hungary. She said in the Voice of America broadcast:

"I worked with all my heart. As a child I always wanted to become a nurse or a surgeon's assistant. I'm religious and take the commandment of brotherly love very seriously. And that exactly is why I escaped."

There is an excessive number of premature births, the nurse declared, attributing this to the communist system of using women for heavy physical labor.

Discussing the hospital situation in Hungary, she explained that a nurse must take care of three or four times as many patients as she did before the communists came to power, with the result that the sick do not receive proper care.

"The patient feels that and becomes irritable," the escapee said in the Voice of America broadcast, "and the nurse who is overloaded with work becomes irritable too. The atmosphere becomes tense. One might say that an atmosphere develops that is typical in the so-called people's democracies."

The name of the nurse, who escaped from Hungary last August, was withheld to protect her relatives behind the Iron Curtain.

N. S. C. C.

Chicago—A dramatic national exposition on employment of the physically handicapped combined with informative speeches, seminars, roundtables and workshops on the vital role of rehabilitation in conquering crippling will be featured at the 1955 annual convention of the National Society for Crippled Children and Adults, Nov. 28-30, at Chicago's Palmer House.

The exposition, the first national exhibit of its kind ever held outside Washington, D. C., will feature on-the-job demonstrations of disabled employees who are on the payrolls of many of the nation's major business and industrial firms. More than 75 prominent companies located in Chicago and in various industrial areas of the U.S. will be among the exhibitors participating in the exposition which will be open free to the public. It will be sponsored by the National Society and both the President's and Illinois Governor's Committees on Employment of the Physically Handicapped.

The theme of the three-day Easter Seal convention is "Conquering Crippling." It will feature many of the nation's top authorities discussing newest methods and latest techniques in treating the crippled through medicine and rehabilitation, as well as on such important related topics as employment, public acceptance, family understanding and voluntary effort.

Edgar Kobak, president of the National Society, will officially open the three-day meeting by introducing three prominent speakers.

They will include A. L. M. Wiggins, chairman of the board, Atlantic Coast Line and Louisville & Nashville Railroad Companes, and president of the Crippled Children Society of South Carolina; Dr. Leonard A. Scheele, surgeon general of the U.S. Public Health Service, and Maj. Gen. Melvin J. Maas, USMCR, Ret., chairman of the President's Committee on Employment of the Physically Handicapped.

Their talks will be followed by the grand opening of the exposition and the day's highlight, an Employers' Luncheon co-sponsored by the Chicago Association of Commerce and Industry. Charles H. Percy, prominent young president of the Bell & Howell Company, Chicago, will be the principal luncheon speaker who will talk on "Odds: 6-1 Against You." Edwin A. Locke, Jr., president of the Union Tank Car Company, Chicago, will be chairman of the luncheon. Music will be provided by the United States Steel Corporation's South Works Male Chorus.

Two afternoon sessions on the opening day of the convention, will also be devoted to employment, with Earl Bunting, vice-chairman of the President's Committee and past-president of the National Association of Manufacturers, moderating a round-table discussion on "Industry and Business Look at the Subject."

George Barr, chairman of the Illinois Governor's Committee on Employment of the Physically Handicapped, will preside at a workshop on techniques for arousing community interest and developing community organization and action. Moderators will include E. B. Whitten, executive director of the National Rehabilitation Association, and Glenn E. Jackson, executive director of the American Board of Certification.

A session for physicians, physical therapists and occupational therapists will feature a clinic demonstration of patients by Dr. Clinton Compere and Associates, Chicago.

Special education will be reviewed by John J. Lee, Ph.D., and Sam Kirk, Ph.D. Dr. Lee, distinguished professor of special education at Wayne University and counselor in the field and past president of the National Society for Crippled Children and Adults, will discuss "Overview and Present Status of Special Education." Dr. Kirk, di-

rector of the institute on research for exceptional children at the University of Illinois, will speak on "Research, Current and Probable Future Developments."

Three nationally-known leaders will lead off the Nov. 29th morning session of the National Society convention. They are Dr. John R. Fowler, Barre, Mass., president of the American Academy of General Practice who will speak on "The Role of the General Practitioner in Conquering Crippling"; Wallace H. Wulfect, Ph.D., chairman of the executive committee, William Esty Company, Inc., whose topic will be "Motivating Volunteers," and John O. Moore, director of the automotive crash injury research department of public health and preventive medicine, Cornell University Medical College, who will speak on accident prevention. Speech rehabilitation and the teen-ager who is crippled will be afternoon seminar topics.

The final morning session of the meeting, Wednesday, Nov. 30th, will feature talks by Mary Switzer, director of the United States Office of Vocational Rehabilitation, Department of Health, Education and Welfare; Harold Boyd, M.D., associate professor of Orthopaedic Surgery, University of Tennessee Medical School; and a "Meet the Press" Conference led by Lawrence Spivak, popular television producer, which will include Meyer Kestnbaum, president of Hart, Schaffner and Marx, and chairman of the Commission on Intergovernmental Relations; Dr. Morris Fishbein, nationally known medical editor and writer, and other selected interrogators.

A Parents' Institute, with James L. Hymes, Jr., Ed. D., Professor of Elementary Education at George Peabody College for Teachers, Nashville, Tenn., speaking on "Helping Children Grow," and a presentation on "Helping Parents Grow" by Lee Gilmore, an American Theatre Wing community play script, will wind up the afternoon of the final day of the convention.

DR. CLARKE NEW SCHERING CHEMIST

Dr. Frank H. Clarke, Jr., has been appointed medicinal chemist in the Medicinal Chemical Research Department of Schering Corporation, Bloomfield, N. J. pharmaceutical manufacturers.

Immediately prior to joining Schering, Dr. Clarke held a post doctorate fellowship in the Chemical Department of Columbia University. Previously he was a member of the teaching staff of New Brunswick University, Fredericton, New Brunswick, Canada, and later research assistant on the National Research Council, Ottawa.

Dr. Clarke holds a baccalaureate degree in chemistry and a master's degree in organic chemistry from New Brunswick University. He received his doctorate in organic chemistry from Harvard University.

Presently residing in Bloomfield, the new Schering appointee is a member of the American Chemical Society, Chemical Society of London, Chemical Institute of Canada, Association of Harvard Chemists, and Phi Lambda Upsilon fraternity.

BONADOXIN CONTROLS 'MORNING SICKNESS' IN 95% OF PREGNANT WOMEN, MDs FIND

Bonadoxin, a combination vitamin pyridoxine and the antihistamine meclizine, was of benefit to 95.7 per cent of 287 women who were given the drug to control nausea and vomiting of pregnancy.

These were the results obtained in a series of clinical trials conducted by Drs. H. H. Groskloss, Miami; C. L. Clancy, Portland, Ore.; E. F. Healey and W. J. McCann, San Rafael, Calif.; F. D. Maloney, Garden City, N. Y. and A. F. Loritz, Chicago. Their findings appear in *Clinical Medicine* (Vol. 2, No. 9)

Good to excellent response to Bonadoxin therapy was obtained in 90.8 per cent of the patients.

The physicians report, "It is apparent, from this study, that it (Bonadoxin) is a worthwhile addition to the physician's therapeutic resources and to the increased comfort of the pregnant women."

According to the investigators, clinical interest in Bonadoxin was aroused by the possibility that this agent might be able to eliminate both the specific cause and general effect of the nausea and the vomiting of pregnancy (commonly called "morning sickness") by combined subjective control and nutritional therapy.

Previously published clinical reports have shown that meclizine is very effective in controlling the nausea and vomiting of motion sickness, and that therapeutic amounts of pyridoxine appear to be necessary to prevent deficiency of this vitamin during pregnancy.

Meclizine dihydrochloride, 25 mg., and pyridoxine hydrochloride, 50 mg., are combined in Bonadoxin, a product of J. B. Roerig & Co. of Chicago.

In this series of clinical trials, dosage of Bonadoxin was arbitrarily set at one tablet taken before retiring. In most resistant cases, an additional tablet was taken upon arising in the morning.

Results were recorded as "excellent" if relief of nausea and vomiting occurred within a few hours, and no later than two days. "Good results indicated a relief of nausea, vomiting, or both after two days, but no later than two or three weeks after therapy was instituted. "Fair" results indicated temporary relief of either nausea or vomiting, or complete relief with residual drowsiness.

The physicians report that of 287 patients, 162 (56.3 per cent) showed "excellent" results; 99 (34.5 per cent) showed "good" results; and 14 (4.9 per cent) had "fair" response.

DRUG MANUFACTURER REMAMED WINTHROP LABORATORIES INC.

New York—The corporate name of Winthrop-Stearns Inc., one of the country's important pharmaceutical manufacturers, has been changed to Winthrop Laboratories, Inc., it was announced here by Dr. Theodore G. Klumpp, president.

Established in 1919 under the name of Winthrop Chemical Company, Inc., the business was consolidated in 1935 with H. A. Metz Laboratories. In 1942, Alba Pharmaceutical Co. was merged with Winthrop and, in 1947, Winthrop-

Stearns Inc. was organized as the result of the acquisition of Frederick Stearns & Co., Detroit.

Winthrop's manufacturing plants are located at Rensselaer, N. Y., and Myerstown, Pa., and it maintains branch offices and warehouses throughout the country. Its research program is carried out at the Sterling-Winthrop Research Institute, also in Rensselaer.

LAKESIDE ORGANIZES NEW SECTION OF ANIMAL CARE

Called Milestone in Laboratory Management at Firm, Section Has Seven Men and Is Headed by E. E. Thebert, DVM

Milwaukee, Wisc.—A new section on animal care has been organized at Lakeside Laboratories, Inc., it was announced by Harvey L. Daiell, M. D., scientific director of the pharmaceutical firm.

He said the development marks a milestone in its laboratory management. Named chief of the new section set up within the pharmacology division, is Ellsworth E. Thebert, DVM, who has just joined Lakeside's scientific staff.

Dr. Thebert heads a staff of seven qualified men. The staff will work in a new wing of the Lakeside plant. This wing is well-lighted and under constant temperature control, it was pointed out. Of modern design, it contains the newest equipment necessary for proper maintenance and nutrition of animals.

The spacious quarters include runways for dogs and a quarantine section for newcomers, where the animals are kept under observation and treated, if necessary, until they are in a normal state of health.

"Lakeside's continually expanding research program necessitates a large animal section," Dr. Daiell explained. "Pharmacologic research requires careful management of the animal section, and the direction of animal care has been assigned to a man well trained in the veterinary sciences."

Dr. Thebert did his pre-veterinary work at Carroll College in Wisconsin and Kansas State College in Kansas, where he received his B. S. and D. V. M. degrees. A native of Rice Lake, Wisc., he served as a bomber pilot in World War II.

His present address is 2204 E. Locust St., in this city.

PFIZER OPENS SOUTHWESTERN DISTRIBUTION CENTER IN DALLAS

Dallas, Texas, Oct. 13—A new Southwestern Distribution Center which will serve a seven-state area, was opened here today by Chas. Pfizer & Co., Inc. in the Brook Hollow Industrial District in the northwest section of the city.

President and Chairman of the Board John E. McKeen and a group of Pfizer executives were hosts at an open house and buffet attended by approximately 250 civic and business leaders and members of hospital and pharmacy groups in the Dallas-Fort Worth area.

To mark the opening, McKeen presented a donation of antibiotics and nutritional products to the Children's Medical Center of Dallas. Chief pharmacist Reuben G. Lewis accepted the drugs in behalf of the Medical Center. Also taking part in the ceremony for the Center, which includes the Bradford Hospital for Babies, the Children's Hospital of Texas, the Morgan Tuberculosis Hospital and the Freeman Memorial Clinic, was James J. Farnsworth, administrator.

The distribution center is the third constructed by Pfizer under its current branch expansion program. A fourth, in Chicago, is under construction and a fifth is planned for the Northwest.

In a short address of greeting, Mr. McKeen said that Pfizer had constructed the new facility to "keep pace with the needs of this fast growing region."

Pfizer, he stated, "is now in a better position to serve its pharmaceutical, chemical and agricultural customers in the area. We are proud to have new roots in the Southwest."

Referring to life-saving drugs such as the antibiotics, McKeen said that society has gained nothing "unless the life we have saved can be lived out with some degree of satisfaction. If people, as they get older, have to live in pain and misery, or have to exist on a near-starvation diet, as many do in foreign lands, we will have failed."

He explained that Pfizer and other pharmaceutical companies are attacking the problem on two fronts. First, he said, they are devoting extensive research to products to treat diseases wich afflict the aged. Secondly, they are developing new and better antibiotic and hormone supplements to speed animal growth and improve feed efficiency, thus making possible more meat at lower cost, he asserted.

The new Distribution Center will be used by Pfizer's four sales divisions—Pfizer Laboratories, the J. B. Roerig & Co., the Chemical Sales and Agricultural Sales divisions. The first two divisions will have regional sales offices in the Center while the other two will for the time being make use of the storage and distribution facilities only.

S. G. Brock will serve as regional sales manager for Pfizer Laboratories while M. A. Javors will head the Dallas sales office for the J. B. Roerig & Co. division. F. C. Goerke has been named branch manager.

NEW COLD PREPARATION TEAMED WITH VITAMINS TO PROVIDE RELIEF, HELP BUILD RESISTANCE

Chicago, Illinois, Oct. 20, 1955—A new cold-relief agent called Coryban has been coupled in a dual package with the multi-vitamin Viterra as a two-phase treatment designed to relieve cold symptoms and to supply vital nutrients. These two products have been formulated by specialists at J. B. Roerig and Co., division of Chas. Pfizer & Co., Inc.

The recently introduced Coryban contains salicylamide, acetophenetidin, caffeine, prophenpyridamine maleate, ascorbic acid and purified hesperidin.

Coryban, according to Roerig's Medical Director Dr. T. A. Garrett, taken at first signs of a cold, may shorten its length. Also, it reduces fever, relieves headaches and quick-

ly relieves other discomforts so often felt during a cold siege. (Viterra is Roerig's time-proven vitamin-mineral combination containing 19 vitamins and 11 minerals in each capsule.)

Coryban's formula provides a three-fold attack to relieve discomfort and promote body defense against colds, Dr. Garrett says.

The salicylamide, acetophenetidin, caffeine group of ingredients will reduce fever, relieve pain and act as a stimulant. Prophenpyridamine an antihistamine, will act to control the stuffy, running nose, so common at the first signs of a cold.

The third group of ingredients, hesperidin and ascorbic acid, are vitally concerned with strengthening the capillary walls and preventing increased capillary permeability.

According to Dr. Garrett, scientists believe that increased capillary permeability permits rapid and widespread penetration of bacteria and virus particles. The causative agent of the common cold is believed to be a virus, or group of viruses.

The Coryban-Viterra package contains a bottle of 30 Viterra capsules and a bottle of 12 blue and white Coryban capsules.

NEW ROERIG SPECIALTY: CORYBAN-VITERRA

What the product is: A packaged combination of new cold relief agent Coryban and the multi-Vitamin and mineral preparation Viterra. Coryban contains salicylamide, acetophenetidin, caffeine, prophenpyridamine maleate, ascorbic acid and purified hesperidin. Viterra contains 10 vitamins and 11 minerals.

What it's for: Dual attack to fight the symptoms of the common cold and guard against vitamin and mineral depletion during this disease. Coryban is designed to reduce fever, relieve headache and other discomforts of the cold. Viterra provides a broad nutritional supplement to help build resistance.

Advantages: Coryban has a three-part formula to relieve discomfort and promote body defense against colds. The salicylamide, acetophenetidin and caffeine ingredients reduce fever, relieve headache and fight drowsiness. Prophenpyridamine, an antihistamine, provides relief from stuffy, running noses so often seen at the outset of a cold. The hesperidin and ascorbic acid protect against increased capillary permeability.

How Administered: Adults—Two capsules of Coryban at the onset of symptoms. One capsule every four hours after initial dose. One capsule of Viterra daily, for 30 days.

Children (6-12 years)—One-half the adult dose. Children under six, as directed by physician.

How it's sold: Coryban-Viterra carton containing bottle of 12 Coryban capsules and bottle of 30 Viterra capsules. Special space saving counter display for Coryban-Viterra available. Coryban is also packaged in a shelf carton display containing 12 bottles of Coryban, 12 capsules per bottle.

Who makes it: J. B. Roerig & Co., division of Chas. Pfizer & Co., Inc., Chicago 11, Illinois.

PARKE, DAVIS & COMPANY REPORTS INCREASES IN SALES AND EARNINGS FOR 9-MONTH PERIOD

Detroit, Oct. 19—Parke, Davis & Company today reported increased net sales and earnings for the first nine months of 1955.

The world-wide pharmaceutical firm said net earnings in the nine-month period of this year totalled $9,528,480, equal to $1.94 on each of the 4,899,457 shares of common stock outstanding and an increase of 35.1 per cent over the same period of 1954.

Parke-Davis reported this amount after deducting and reserving during that period $863,445, equivalent to 1955 local net earnings to date in Argentina. Had such earnings been included, as they were in prior years, consolidated net earnings for the first nine months of 1955 would have been $10,391,925, or $2.12 a share.

Last year, the company pointed out, the nine-months report showed net earnings of $7,052,264, equal to $1.44 per share.

Net sales for Parke-Davis during the 1955 nine-month period totalled $90,219,176, representing an increase of 12 per cent over the $80,568,841 for the same period in 1954.

During the third quarter of 1955, Parke-Davis had sales of $30,428,-370 and earnings of $3,134,617. This compared with sales of $27,-983,890 and earnings of $2,494,-749 during the same three-month period in 1954.

The company, which has made a profit every year since 1876, will pay its 272nd consecutive dividend on Oct. 31 to more than 25,000 stockholders of record Oct. 10. It will amount to 35 cents per share, the fourth such payment this year.

NEW COMPREHENSIVE APPRAISAL OF "REACTIONS" TO MERCURIAL DIURETICS PUBLISHED IN *ANNALS OF ALLERGY*

"When is a 'reaction' not a reaction?"

This is one of the interesting questions discussed in a new and stimulating, comprehensive evaluation of the extensive literature on reactions to mercurial diuretics during twenty years, published in the *Annals of Allergy* (13:131, 1955).

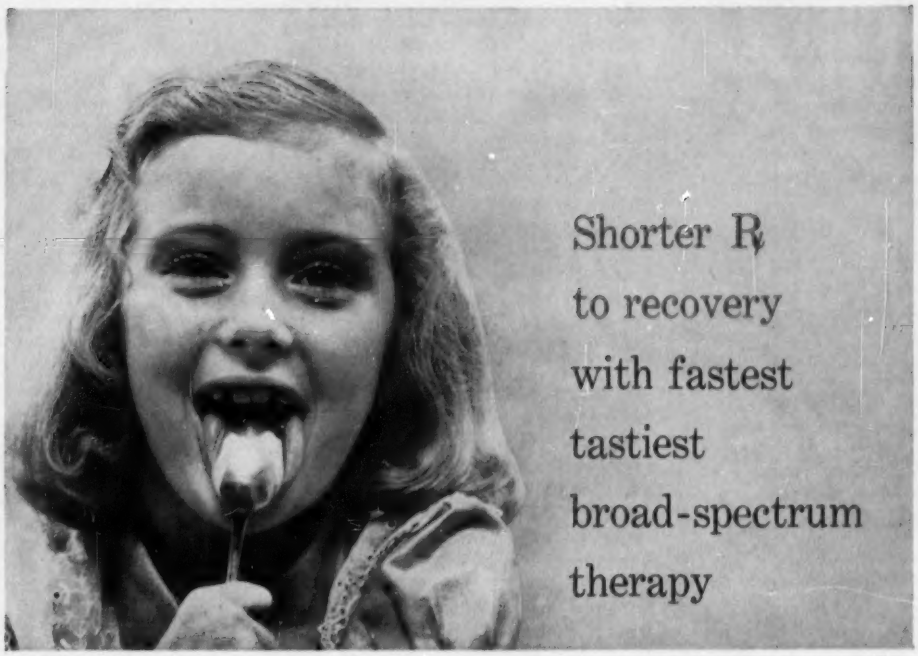
Author of the paper, virtually a monograph, with a bibliography of 105 references, is Ethan Allan Brown, M. D., director, The Asthma Research Foundation, Boston.

The paper is called "The Question of Reactions to Mercurial Diuretics, A Reappraisal."

Dr. Brown covers mode of administration; dosage and management; distinctions that must be drawn among the drugs, including the newer oral agents; and various reactions.

"Any appraisal of the literature concerned with reports of reactions to mercurial diuretics must take into consideration factors other than the drug itself," he points out in a section called "The Patient Or The Drug?"

He suggests particularly the more judicious application of other measures commonly employed concurrently in therapy, such as restricted salt diets. He concludes also that some reactions observed in the past



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NEW STANDARDS FOR TETRACYCLINE THERAPY IN NEW READY-MIXED LIQUID FORM

Pfizer PFIZER LABORATORIES, *Division, Chas. Pfizer & Co., Inc.*, Brooklyn 6, N. Y.

have been due not to the "toxicity" of the mercury in preparations as such but to the hypersensitivity of certain individuals.

"A number of reactions frequently attributed in the literature to mercurial diuretics are not truly due to the drug, but... are the results of diuresis causing sodium, potassium or calcium deficiency," he states.

"The advent of the newer organic mercurial complexes, with the use of intramusclar, subcutaneous and oral administration, more cautious dosage schedules and the judicious awareness of the implications of early minor side reactions" is offered as the explanation of the surprisingly few reports of reactions in recent years.

TYZINE PROVIDES "EXCELLENT" RELIEF FROM NASAL CONGESTION IN ALL BUT ONE OF 204 PATIENTS, MD REPORTS

Tyzine, a nasal decongestant, obtained excellent results in 203 of 204 patients treated By Dr. Isidore Neistadt of Valley Stream, New York, according to a report appearing in the *A.M.A. Archives of Otolarynology* (Vol. 62, No. 2).

The decongestant (tetrahydrozoline hydrochloride — Pfizer) was tested on 12 patients with allergic rhinitis and 192 with nasopharyngitis or sinusitis, or both.

"Results were excellent in all but one patient, whose response was only partial," Dr. Neistadt said. "Besides this high effectiveness, tetrahydrozoline displayed the notable advantages of prolonged action and absence of untoward effects, local or systemic."

The investigator reported that relief appeared immediately ofter instillation of a 0.1 per cent Tyzine solution and lasted from four to 24 hours. About 90 per cent of the patients had relief for periods up to or exceeding eight hours, Dr. Neistadt found.

"This means that the effect of a bedtime instillation generally lasted through the night, without return of congestion causing wakefulness to instill more drops before morning," he said.

In this test series no patient awakened because of need of further drops of Tyzine. One patient had suffered from local irritation on using all other nose drops, but found Tyzine nonirritating, the clinician reported. Four of the patients said that Tyzine was the only nasal decongestant that they had found effective at all.

According to Dr. Neistadt, none of the significant side-effects, local or systemic, previously mentioned by patients as common with other effective nasal decongestants were produced by Tyzine in this series.

The group of 204 patients consisted of 96 males and 108 females ranging in age from 19 months to 77 years, including 12 children, none of whom was older than six years. Dosage in all cases was five drops in each nostril four times daily. The duration of treatment ranged from four to 16 days, with an average of 10 days.

GRAVE SHORTAGE OF RURAL HEALTH SERVICES

Top Pan American Health Authorities Discuss Training of Public Health Personnel

Medical care in rural areas and the education of public health personnel were this year's subjects for the technical discussions held during the Eighth Meeting of the Pan American Sanitary Organization's Directing Council, which sits also as the Regional Committee of the World Health Organization. Such discussions have taken place at annual PASO meetings since 1951, following the pattern established by the World Health Assembly in 1949. These gatherings of health professionals from many countries afford an unusual opportunity for an exchange of views on subjects normally outside the scope of the regular agenda.

The shortage of public health personnel is felt in most countries of the world, and nowhere so keenly as in the rural areas. It is perhaps difficult for city-dwellers to realize that over two-thirds of the world's population live in technically less developed, largely rural, areas, that their life expectancy at birth averages only 30 years, in contrast with 63 years in the more favored countries, and that their average annual per capita income is under 50 dollars.

Poverty helps to create more disease, which, in turn, tends to perpetuate poverty. It is a challenge of our times to apply properly the technical advances now available to combat such communicable diseases as typhus, yellow fever, malaria, tuberculosis, and the treponematoses, and thus bring to this large group of people an improvement in health without which they are unlikely to realize their full social, cultural and economic potentialities. It should be added that the improvement of environmental sanitation is fundamental to any advance.

At the invitation of the Director of the Pan American Sanitary Bureau, Dr. Fred L. Soper, two papers had been prepared in advance: "Methods of Improving the Education of Public Health Personnel" by Dr. José Bustos, Chief of the Coordinated Public Health and Welfare Services of the State of Veracruz, Mexico; and "Medical Care in Rural Areas," by Dr. J. A. Diáz Guzmán, Chief Medical Officer in the Division of Rural Health of Venezuela's Ministry of Public Health and Welfare. These papers covered a wide field. The health experts, who had only two days at their disposal to discuss these topics, decided to confine themselves to specific aspects of the problems and to relate their remarks to the resources available in the various countries, rather than to discuss ideals beyond the reach of many governments at the present time.

Methods of Improving the Education of Public Health Personnel

Most of the discussion was focused on *in-service* training. Some closely related points, including problems of recruitment, stability of appointments, and the creation of a true public health career system were also mentioned. A properly balanced relation between in-service training and academic education was emphasized, and several speakers drew attention to the fact that while some universities in the Americas offer a very high standard of training in their public curricula, others do not offer an adequate program. Education should be geared to local conditions, it was agreed; long in-

struction on the intricacies of highly advanced water filtering systems, for instance, might be out of place in areas where basic sanitation and excreta disposal had yet to be developed. Such regions required large numbers of general public health workers trained to meet these relatively basic problems.

A discussion of the principles and objectives behind in-service training led to the assertion that all personnel who work in any public health program must be familiar with the fundamental philosophy behind it, as well as with the necessary techniques; one of the primary objectives must be the development of an understanding of the value of team approach, since a good team spirit among workers in a health department facilitates the cooperative planning, execution, and evaluation of programs.

In connection with the categories of personnel which should be included in in-service training programs, and the methodology to be employed, there was general agreement that training programs of some type should embrace *all* the staff, professional, sub-professional (including auxiliaries and non-technical personnel of all types), and administrative. Due distinction would, of course, have to be made between the needs of newcomers and existing staff.

There was a variety of opinion as to how extensive the program of in-service training should be, but there was general agreement on the need for regular refresher courses to keep personnel abreast of technical advances and, if necessary, of modifications in the guiding principles.

It was also agreed that in every county certain centers should be set up as primary teaching centers. One such center should have the function of coordinating the teaching and setting of standards for the other centers in the different regions of the county. The desirability of having a director and coordinator of in-service education programs at the national level was emphasized.

Finally, the experts considered the various methods of instruction, including: classroom teaching and demonstrations with audio-visual aids, supervised field experience, case studies, round-table discussions, lectures by special consultants, socio-dramas, and the use of literature outlining recent developments. It was stressed that all participants in these methods of instruction should be encouraged to express their own views and experiences, and thus at the same time contribute to a critical analysis of the health program itself. In the long run, improvement of the health services would be the best demonstration of the effectiveness of in-service education programs.

Medical Care in Rural Areas

In discussing medical care in rural areas the experts acknowledged the impossibility, in practice, of separating preventive and curative

medicine, each country having to use its own methods to integrate these two aspects and to obtain an adequate balance between the various health activities.

The obvious interaction and dependency that exist between urban and rural areas was noted; it would be unrealistic to hope to have good medical services in rural areas if they were lacking in the towns. In practice, the various national organizations are unable to provide over-all public health services in the same degree at all levels; and the present lack of public health resources at the rural level is expected to continue for some time in many countries.

It was fully recognized that rural health centers should be integrated with those in the towns. In this way, advantage can be taken of some facilities that need to remain centralized, while other services would profit from decentralization to the rural level. Through this system the frequently-repeated ideal would progressively be achieved, according to which no citizen, under any circumstances, should be deprived of the best resources that modern medical science, preventive as well as curative, can provide to prevent suffering, disability and death.

Light was shed on the importance of rural areas in the majority of the American countries, because of their social, demographic, and epidemiologic influence on national health conditions, and because of the lack of health services in such areas. There was unanimous agreement that adequate care of the rural population involves a normative and supervisory agency with competent, full-time personnel, operating within the national or state public health service. The need for workers to cooperate closely with all other departments concerned with the social and economic welfare of the rural population is vital. This could be aided by the formation of local health committees on which officials, the clergy and persons of local prestige could serve.

It was agreed that minimum health services in rural areas should include the following: environmental sanitation, with emphasis on water supply and excreta disposal; control of infecto-contagious diseases; maternal and child health; medical care, including consultation and hospitalization; statistical services, with emphasis on the medical certification of causes of death; laboratory facilities; and health education.

The minimum personnel requirement for a health center should be one public health officer-physician; a nurse, if possible: two clinic auxiliaries, one of them a midwife: one auxiliary in sanitation and statistics; one service employee; and a chauffeur (if there are ambulances).

The personnel who are to work in rural health centers should be as adequately trained to perform their specific duties as their urban counterparts. Working conditions, including salary, opportunities for advancement, security, and housing would have to be made as attractive as possible. Supervision and encouragement should not be neglected.

The financing of rural health facilities is one of the major factors influencing their development. It was agreed that this must depend

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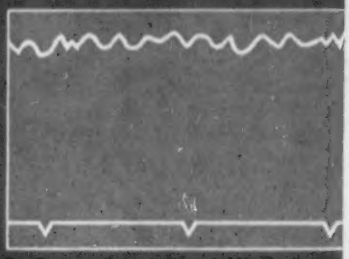
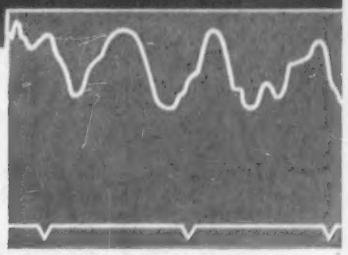


1. Contractions without Mucilose



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principally on allotments from the national, state, and regional budgets. Other sources worthy of consideration are: municipal governments, Social Security extended to rural areas, and private concerns and individuals. The community that is served can do its share by paying for curative serices and through voluntary service sanitation projects and other preventive works.

Next Year's Topic

The Directing Council has selected Guatemala City for its next annual meeting in the fall of 1956. The technical discussions at that time will be on the subject "Methods for the Preparation of National Public Health Plans."

PREDICTS "GREAT AND SIGNIFICANT PROGRESS" IN MEDICINE DURING NEXT FEW YEARS

Big Rapids, Mich.—A prediction of "great and significant progress in the conquering of diseases as yet uncontrolled" was made here by Carl Johnson, United States and Canadian sales manager of Parke, Davis & Company.

Speaking at the banquet of the third annual pharmaceutical seminar at Ferris Institute, where he was graduated in 1926, Johnson referred to vast amounts being spent for medical research, and added:

"Money alone won't account for the quickened tempo which will be so obvious to us in the period just ahead. A very lively rivalry within the industry—with intensified competitive pressure—is spurring on new product development and process development to a faster pace than ever before."

He urged the pharmacists to "sell" the general public on "the bargain they get in daily medical care."

Johnson said, "It is true that some therapeutic agents cost more today than before, because they are more specific and have been introduced through many years of research, all of which costs money to develop.

"But the total economic cost of an illness has dropped sharply."

Pharmacists must strive to increase their professional stature with the public, the Parke-Davis executive added.

"A sound first step in attaining good relations with the ultimate consumer is to recognize that—up to a certain point at least—his interest in medical matters is natural and legitimate.

"Another way to exhibit a tolerant and professional attitude is by being willing and ready diplomatically to discuss honest 'gripes' and complaints, wheather they apply to physicians, to the price of prescriptions, or imply a criticism of some pharmaceutical manufacturer.

"Another way: by encouraging our fellow pharmacists to adopt a board-gauged attitude toward matters affecting any branch of medicine."

Increasing professional stature, he said, isn't just something that is nice to do; it is something we must do—all of us. We owe it to ourselves and to the feeling inside of us that made us take up pharmacy in the first place."

REST COMES BEST to the relaxed patient.

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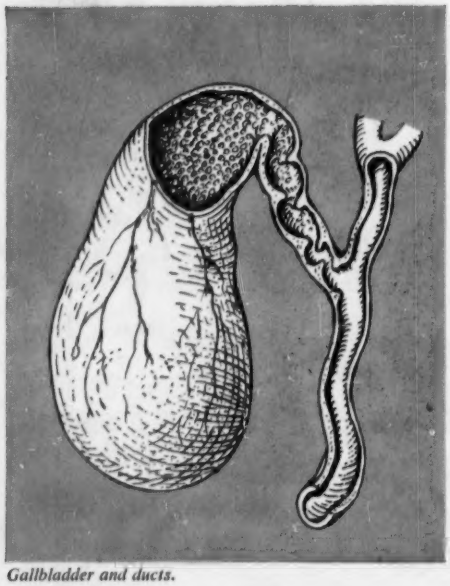


Gallbladder and ducts.

The ketocholanic acids in Ketochol stimulate the flow of hepatic bile and flush the bile ducts. Antispasmodic medication, as provided in Pavatrine, diminishes gastrointestinal irritability and, by relaxing the sphincter of Oddi, effectively reduces symptoms of colic. This therapeutic program offers rational, conservative therapy in gallbladder dysfunction.

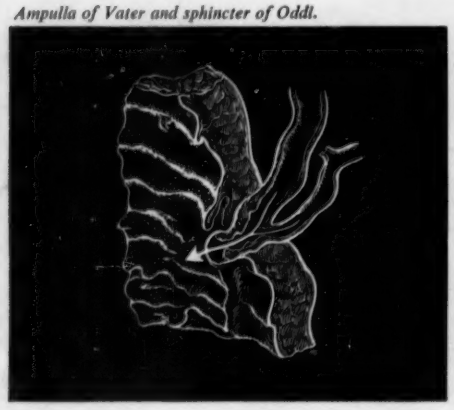
That the four bile acids present in Ketochol relieve biliary stasis is even more definitely proved by their use in the diagnosis of nonvisualized gallbladders. After the administration of Ketochol, repeat cholecystograms permitted[1] correct diagnoses.

In conjunction with the foregoing medication, proper diet, adjusted intake of milk and cream and mental relaxation are important.

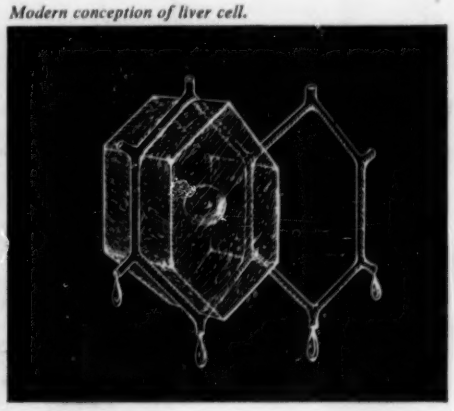
The average dose of Ketochol is one tablet three times daily with or following meals. The average dose of Pavatrine or Pavatrine with Phenobarbital is one or two tablets three or four times daily as needed. G. D. Searle & Co., Research in the Service of Medicine.

1. Berg, A. M., and Hamilton, J. E.: A Method to Improve Roentgen Diagnosis of Biliary Diseases with Bile Acids, Surgery *32*:948 (Dec.) 1952.

Ampulla of Vater and sphincter of Oddi.



Modern conception of liver cell.



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